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# Archives of Neurology and Psychiatry

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## INTRAMEDULLARY TUMORS OF THE SPINAL CORD

A REVIEW OF FIFTY-ONE CASES, WITH AN ATTEMPT  
AT HISTOLOGIC CLASSIFICATION \*

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Tumors of the brain are studied more and have been more satisfactorily classified within recent years than formerly. This is due, in great part, to the contributions of Cushing, Bailey and their co-workers, as well as of several other groups of investigators, especially in America. However, in neurologic and neurosurgical clinics, intramedullary tumors of the spinal cord are encountered much less frequently than tumors of the brain, so that the types are less thoroughly studied. The structure of the spinal cord is essentially the same as that of the brain; therefore, one would expect at least some similarity among the neoplasms arising from them.

It is our aim in this study to classify fifty-one tumors in which sufficient tissue has been removed to make classification possible and to endeavor to correlate the clinical and surgical features with the histologic structure of the neoplasms. A review of the clinical features that were presented in these cases disclosed nothing new. Excluding caudal tumors, which involved the conus, intramedullary tumors were more common in males than in females. The average duration of symptoms was four and nine-tenths years, which is considerably longer than the duration of symptoms in cases of extradural and extramedullary tumors. In three cases there had been paraplegia in flexion, although in two of these the patellar reflexes could be obtained. In two, the Brown-Séquard syndrome was well marked. In two others, choked disks were found, and in one of these, homonymous quadrantanopsia. The Wassermann reaction of the spinal fluid of one patient was strongly positive, but there were no indications of syphilis.

It was often impossible to distinguish between intramedullary and extramedullary tumors preoperatively, and sometimes differentiation

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\* Read at the Fifty-Sixth Annual Meeting of the American Neurological Association, Atlantic City, N. J., June 10, 1930.

was difficult even at operation. A dissociated, waistcoat type of sensory disturbance and a marked difference in levels of various sensory disturbances, of course, suggested intramedullary tumor. Excluding those cases in which the conus and the cauda were involved, the following features were noted in the cases of intramedullary tumors: involvement of lower motor neurons was present in 40 per cent of cases; root pains referred to a distance from the spinal column, present in 48 per cent, were less common than when extramedullary tumors were present; spinal pains, present in 72 per cent, were much more common than in cases of extramedullary growths; tract pains, present in 6 per cent, represented about the same incidence in both types. When the intensity of perianal sensibility differed from that at higher segmental levels, relative preservation of perianal sensibility was present. These phenomena were present in more than half of the cases. However, relative preservation of perianal sensibility was found to be about four times as common in cases of extramedullary tumors. The existence of spinal block, or of xanthochromia, was of little aid in distinguishing intramedullary from extramedullary tumors. Iodized poppy seed oil 40 per cent which was employed in one case, disclosed splitting of the stream at the level of the tumor.

In only a few cases could the tumor be removed completely; in many, however, operation relieved the patient of pain, and in some cases, splitting of the cord along its dorsal aspect and partial removal of the tumor resulted in temporary improvement. Of a total of ninety-one intramedullary tumors, sufficient tissue was removed in fifty-one to allow satisfactory investigation and consequent inclusion of the tumors in this series; in the forty others, either decompression only was done or insufficient tissue was removed to allow the tumors to be included in this study. Moreover, tumors that arose from the filum terminale have not been included in spite of the fact that they belong in the group of gliomas; they will be considered in a separate study. Several other borderline types are not included, such as cysts of the spinal cord, although they frequently were associated with tumors. In another case, a medulloblastoma of the cerebellum extended downward and invaded the medulla oblongata and upper part of the cervical portion of the spinal cord, giving some symptoms of a tumor high in the cervical portion of the cord, but because it was not primary in this situation, it has not been included in this series. One group included in this study consists of three cases in which the neoplasms were completely removed from the subarachnoid space. The tumors, although extramedullary, were gliomas, and because of this fact and because their origin is obscure, they have been included in this series. The growths were attached to the pia, and their origin could not be traced to the substance of the spinal cord. Such tumors are uncommon, and it is not certain that they did not originate in the spinal cord, attached by

a pedicle, and that they became detached later. However, since the three patients from whom these tumors were obtained recovered, complete investigation was not possible. Gliomas may originate in the subarachnoid space. In the last few months, four cases have come under our observation in which heterotopic masses of glial or ependymal tissue, or both, were situated in the subarachnoid space of the medulla and spinal cord (fig. 1 *A*). It is possible for neoplasms to originate from such masses.

A satisfactory classification of intramedullary tumors of the spinal cord has not been suggested, since most cases are recorded in isolated

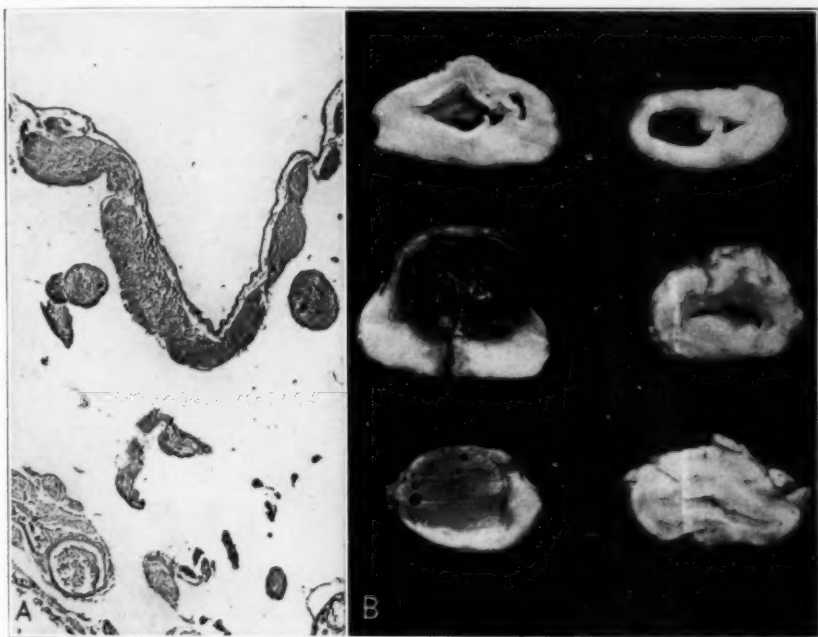


Fig. 1.—*A*, heterotopic masses adherent to the arachnoid, in the subarachnoid space, and adherent to the wall of a vein (thionin;  $\times 40$ ); *B*, sections of a spinal cord with two intramedullary tumors associated with syringomyelia. The syringomyelic cavity is duplicated in places.

reports or in small groups. The names that have been suggested are so various that it is impossible even to attempt classification of those tumors of which reports have accumulated in the literature, particularly those of parenchymatous origin. In this study, we had tissue available from fifty-one cases. These cases may be divided into two main groups: those of parenchymatous origin and those arising from the interstitial substance. More attention has been paid to those of nonparenchymatous origin, and their types are now well understood.

As in gliomas of the brain, many tumors of the spinal cord contain several types of glial cells at different stages of differentiation. In gliomas of the spinal cord this tendency is more marked, and it is the rule rather than the exception to find mixed tumors. This is particularly true in the group of ependymomas, in which the characteristic cell structure and arrangement are intermingled, but in addition the ependymal cells show a tendency to differentiate into the more mature astroblasts and even oligodendroglia. It is unfortunate that the fixation and the small pieces of tissue available prevented use of some of the more specific stains; and so at times we had to rely on the stains used as a routine measure.

Of the parenchymatous tumors, by far the most common are those of ependymal origin, which probably arise from the remnants of the central canal.

#### EPENDYMAL TUMORS

Ependymal tumors are uncommon in the nervous system. Among 254 classified gliomas, Bailey and Cushing<sup>1</sup> reported 7 ependymomas, whereas in this series of intramedullary tumors of the spinal cord, there are 21 (42 per cent). There are three definite types of cellular arrangement in this group of 21. However, it is unusual to encounter a tumor in which the structure is limited to one type. Usually two, and sometimes all three, types are represented in each neoplasm, but for purposes of classification the dominant cell arrangement is used.

In our series there are six tumors of the first type, in which many canals lined with ependyma are seen (fig. 2 *A* and *B*). These canals simulate the ventriculus terminalis or a dilated central canal with ingrowths covered with ependyma. The cells, however, are more columnar and larger than normal. The nuclei are larger, and sometimes more hyperchromatic, but few, if any, mitotic figures are present. The canals are either empty or contain some debris, and, as a rule, mucus is not present. Blepharoplasts (Bailey)<sup>2</sup> are present in many cells between the nucleus and the base, but cilia are not seen in any of these tumors. In one case, the tumor was composed in part of irregular channels, with papillomatous ingrowths which simulate markedly a characteristic of papilloma choroidium, except that in the tumor under consideration the cells are less columnar in type than those seen in papilloma choroidium. The papillomas have a core of connective tissue, with capillaries, and are covered with a layer of ependymal cells—

1. Bailey, Percival, and Cushing, Harvey: *A Classification of the Tumors of the Glioma Group*, Philadelphia, J. B. Lippincott Company, 1926, p. 175.

2. Bailey, Percival: *A Study of Tumors Arising from Ependymal Cells*, *Arch. Neurol. & Psychiat.* **11:1** (Jan.) 1924; *Quelques nouvelles observations des tumeurs ependymaires*, *Ann. d'anat. path.* **2:481**, 1925.

sometimes two or three layers—which have a tendency to arrange themselves around blood vessels, with processes adherent to the adventitia.

There are eight tumors of the second type in which there is little, if any, attempt to form canals, but in which the cells form a solid mass. However, the cells have a tendency to arrange themselves around blood vessels, and with the hematoxylin and eosin stain the vessels appear to be surrounded by a homogeneous eosin-staining zone (fig. 3 *A*). With Mallory's phosphotungstic acid hematoxylin or with the iron hematoxylin stain (fig. 3 *B*), this zone is seen to resolve itself into

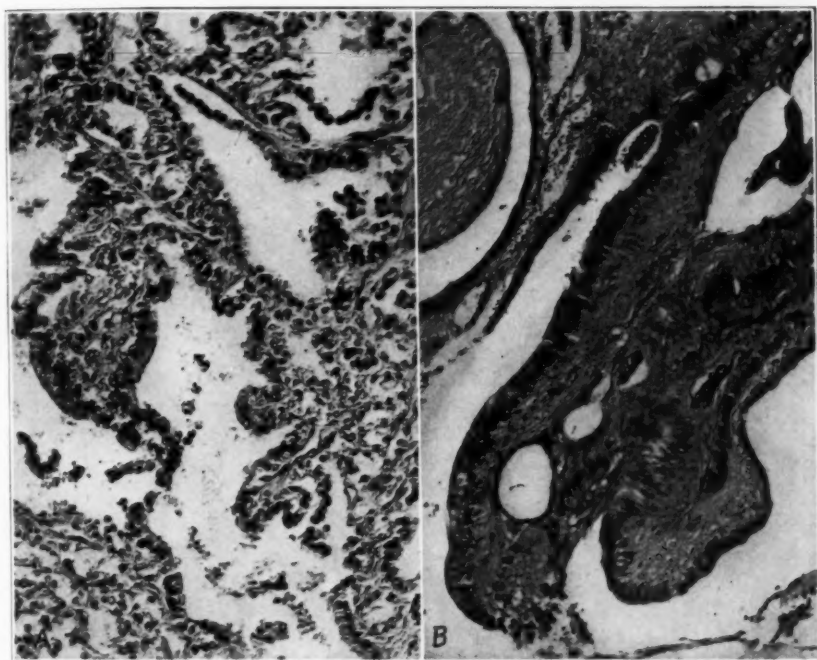


Fig. 2.—Ependymomas in different cases. Both simulate ependyma-lined cavities such as the ventriculus terminalis. The stroma is different in each tumor; *A*, hematoxylin and eosin;  $\times 150$ ; *B*, hematoxylin and eosin,  $\times 90$ .

numerous processes coming from the cells and extending into the perivascular space (fig. 4 *A*). The nuclei of the cells in these tumors are usually oval, they contain several chromatin granules, and the cytoplasm is abundant. The cytoplasm streams off, forming one or two processes, which are heavy. One of these processes often ends around a perivascular space, whereas the other, equally heavy, extends into the surrounding tissue. The latter process frequently tapers off gradually, but more often has an abrupt, frayed termination, quite unlike the processes of astroblasts. There is little, if any, tendency to inter-

lacing of fibrils as in the spongioblastoma unipolare. Mitotic figures are not seen in any of these tumors. This is the only type of ependymoma in which an entire neoplasm is composed of one type of cellular arrangement, although most have a tendency to form a few small tubules (fig. 3 *A*).

The third type of ependymal tumors is one about which there is some doubt. It simulates closely the type of neoplasm known as a neuro-epithelioma, which Penfield<sup>3</sup> claimed to be ependymoma, and Roussy and Cornil<sup>4a</sup> and Roussy, Lhermitte and Cornil<sup>4b</sup> called ependymoglioma. In

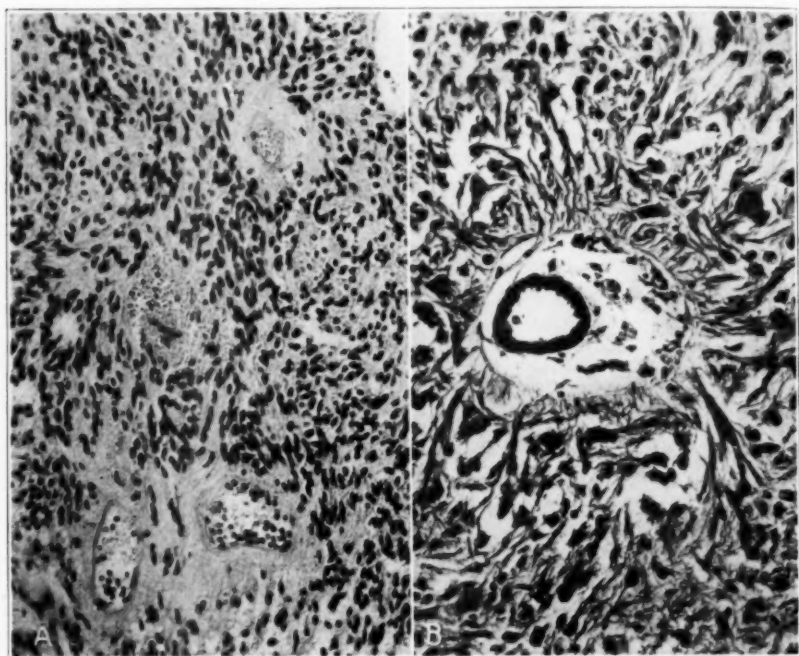


Fig. 3.—*A*, ependymoma of the solid cell type but with the formation of tubules or rosettes. There are homogeneous areas around the blood vessel (hematoxylin and eosin,  $\times 150$ ). *B*, ependymoma with perivascular processes; some cells have processes extending away from the wall of the blood vessels (iron hematoxylin;  $\times 250$ ).

this series of tumors there are seven such neoplasms. These, as in the two previous groups, are not entirely limited to one type of cellular arrange-

3. Penfield, Wilder: *Principles of the Pathology of Neurosurgery*, Nelson Loose-Leaf Living Surgery, New York, Thomas Nelson & Sons, 1927, vol. 2, chapter 6, pp. 303-347.

4a. Roussy, G., and Cornil, L.: *Tumeurs cérébrales*, in Roger, G. H.; Vidal, F., and Teissier, P. J.: *Nouveau traité de médecine*, Paris, Masson et Cie, 1925, vol. 19, pp. 467-579.

4b. Roussy, G.; Lhermitte, J., and Cornil, L.: *Essai de classification des tumeurs cérébrales*, *Ann. d'anat. path.* 1:333, 1924.

ment, but are mixed. The characteristic cellular arrangement is that of rings which vary much in size (fig. 4 *B*). The cells are small and have nuclei without much chromatin, and the cytoplasm is scanty and only slightly granular. Cell processes are not common where this cellular arrangement prevails. There seems to be a pseudobasement membrane with the cells outside of it, and within the pseudomembrane there is a substance which often has a purplish reaction with hematoxylin and eosin, but which gives a specific reaction for mucus with a mucicarmine stain. Blepharoplasts are present in many of these cells, but cilia are not seen.

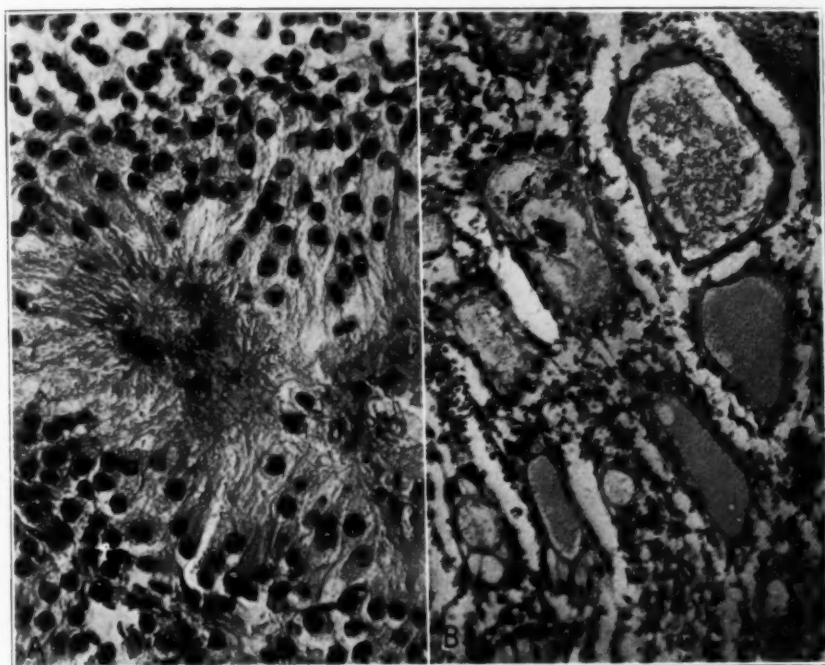


Fig. 4.—*A*, ependymoma of the solid cell type with perivascular processes (hematoxylin and eosin;  $\times 350$ ); *B*, ependymoma of the neuro-epitheliomatous type. The acinar arrangement with pseudobasement membrane and the epithelial cells on the outside of this membrane are evident. This is one of the tumors in the subarachnoid space (hematoxylin and eosin;  $\times 150$ ).

Those parts of the tumors in which the cells are arranged in rings somewhat simulate normal thyroid gland, with the acini filled with colloid, except that the pseudobasement membrane is between the epithelial cells and the colloid and not outside the ring of cells. In other parts of some of these tumors the cellular arrangement is papillomatous and not acinar, with the core of the papilloma made up of tissue that gives a reaction for mucus instead of being composed of blood vessels and

connective tissue. In parts of the tumors in which the cells do not form rings, the solid cell type of ependymoma is most common, with the cells arranged around blood vessels, as in that type of tumor. The cytoplasm is more abundant and granular. Mitotic figures are not present.

#### SPONGIOBLASTOMAS

Spongioblastomas are less common than they would be in a similar series of neoplasms of the brain. There are only seven such tumors in this series, and they are all of mixed types (fig. 5 *B*). They con-

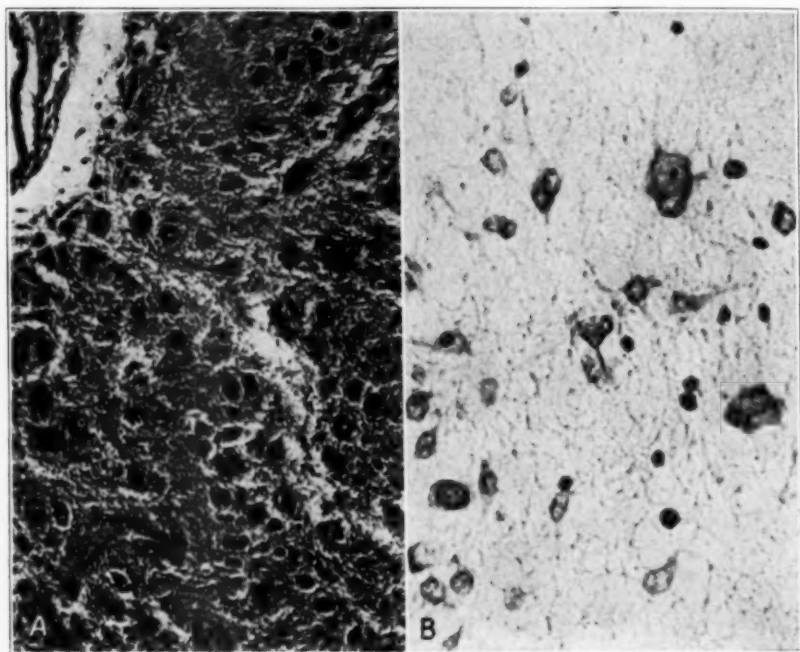


Fig. 5.—*A*, ganglioneuroma, the cell type with large vesicular nucleus. Some dendrons are impregnated. The characteristic cellular distribution is shown (silver impregnation;  $\times 200$ ); *B*, mixed tumor with spongioblasts and neuroblasts. The spongioblasts predominate, so it is a spongioblastoma (thionin;  $\times 400$ ).

tain unipolar, multipolar (astroblasts) and some bipolar cells. Few fully differentiated astrocytes are present. Two contain medulloblasts, and in three, neuroblasts are present. These neuroblasts are unipolar or multipolar, but there are no adult ganglion cells. In two tumors, small masses of ependymal cells are present. It is unusual to find so many types of cells in one neoplasm; this is especially true in our experience with neoplasms of the brain. Although bipolar cells are present,

these tumors do not simulate spongioblastoma multiforme of the brain in any way, nor do they have any resemblance to spongioblastoma unipolare. They have no exact replica in the brain, although we recognize that medulloblastomas have a tendency to differentiate into neuroblasts or spongioblasts, but rarely into both in the same tumor. Because these tumors are composed of so many types of cells in which various spongioblasts predominate, we shall classify them under the general term of spongioblastoma until more information or material is available and an ultimate classification or subdivision can be offered.

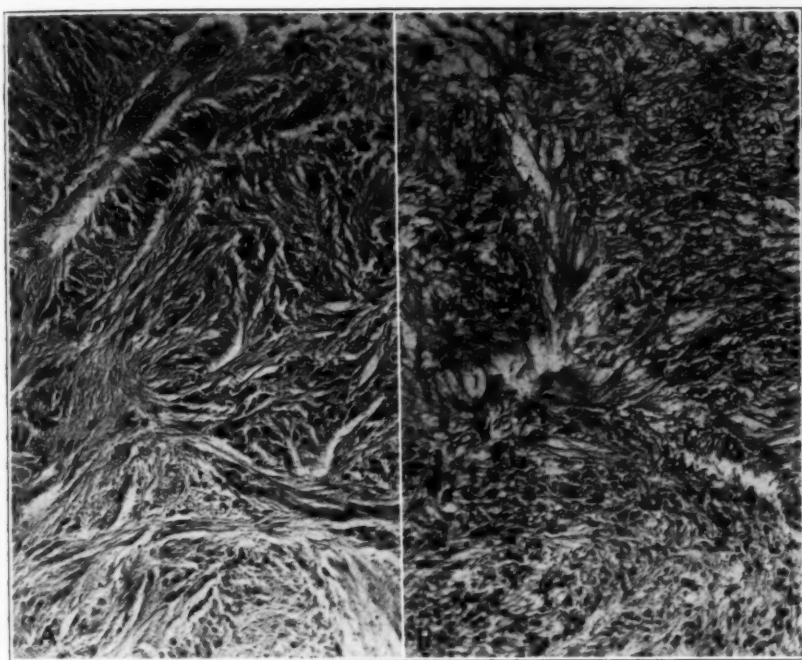


Fig. 6.—*A*, spongioblastoma unipolare. This is a characteristic picture. It has a similarity to a neurofibroma, but there are early vascular processes (hematoxylin and eosin;  $\times 100$ ). *B*, astroblastoma. This is not a very characteristic photograph, for other areas of the same tumor are more fibrous; perivascular processes and fine processes from some cell bodies are present (hematoxylin and eosin;  $\times 125$ ).

#### UNIPOLAR SPONGIOBLASTOMAS

Two tumors in this series we classify as unipolar spongioblastomas. They are characteristic, judged by the standards laid down by Bailey and Cushing. There is a definite resemblance to neurofibroma in that the tumors are fibrous, have a tendency toward interlacing of the fibrils

and even occasional palisading of the nuclei. However, the palisading is by no means perfect, the nuclei are not narrow and elongated, and the fibrous whorls are loose in texture (fig. 6 *A*). Occasionally the cells show a tendency to send processes toward blood vessels, but the vascular feet are imperfect. This suggests a tendency toward further differentiation into astroblasts, but if they are present, they are difficult to recognize. As pointed out by Bailey,<sup>5</sup> most of the cells are not unipolar, but bipolar; they send out processes from both ends of the cells; these processes are distinct, and many are subdivided. There is no difficulty in distinguishing this type of tumor from perineural fibroblastomas or from bipolar spongioblasts seen in the spongioblastoma multiforme or in our mixed group of spongioblasts. Mitotic figures are absent, and the tumor has essentially a benign appearance.

#### SPONGIOBLASTOMA MULTIFORME

It is an interesting fact that at least a third of all gliomas of the brain are spongioblastoma multiforme and that only one, at least so designated, has been described as occurring in the spinal cord. This description appeared in the original contribution of Globus and Strauss.<sup>6</sup> We naturally wonder whether the tumors have been described under some other name. The giant cell glioma of Straube has many characteristics of spongioblastoma multiforme, although as late as last year Slater and Reynolds<sup>7</sup> described a giant cell glioma and claimed that the many nuclei present in their tumor were not surrounded by cell bodies, but that they were nuclei in a syncytial mass. In our series, four such tumors occurred; at least they are true to type as far as their nuclear characteristics, and in parts their cellular characteristics, are concerned. However, with Mallory's phosphotungstic acid hematoxylin stain, definite glia fibrils are seen, and with the Cajal gold chloride stain, cellular bodies are demonstrated. The nuclei are markedly variable in size, and some giant nuclei are seen (fig. 7 *B*); this would correspond to the nuclei of spongioblastoma multiforme; on the other hand, in three of these cases few mitotic figures are present, in spite of the marked hyperchromatism of the nuclei. The fourth case is that of a typical spongioblastoma multiforme, such as one sees in the brain, with giant cells, mitosis, regions of necrosis, etc. (fig. 7 *A*). In the other three cases, the blood vessels are not entirely characteristic of those usually seen in spongioblastoma multiforme, although endothelial activity is present however to a smaller degree than in the classic tumor,

5. Bailey, Percival: Further Remarks Concerning Tumors of the Glioma Group, *Bull. Johns Hopkins Hosp.* **40**:354 (June) 1927.

6. Globus, J. H., and Strauss, Israel: Spongioblastoma Multiforme, *Arch. Neurol. & Psychiat.* **14**:139 (Aug.) 1925.

7. Slater, J. K., and Reynolds, F. E.: A Study of a Case of Cervical Glioma, *Brain* **52**:425 (Dec.) 1929.

and areas of necrosis are not common.\* Many of the cells have the appearance of bipolar spongioblasts, although other types of spongioblasts also are present. We suggest that these tumors are at least closely allied to spongioblastoma multiforme, although the cells are more differentiated and the tumors are less malignant.

#### ASTROBLASTOMAS

In a recent contribution, Penfield and Young<sup>8</sup> described an intramedullary tumor found in a case of Recklinghausen's disease in which an ependymoma coexisted with a cellular astrocytoma. In two of our

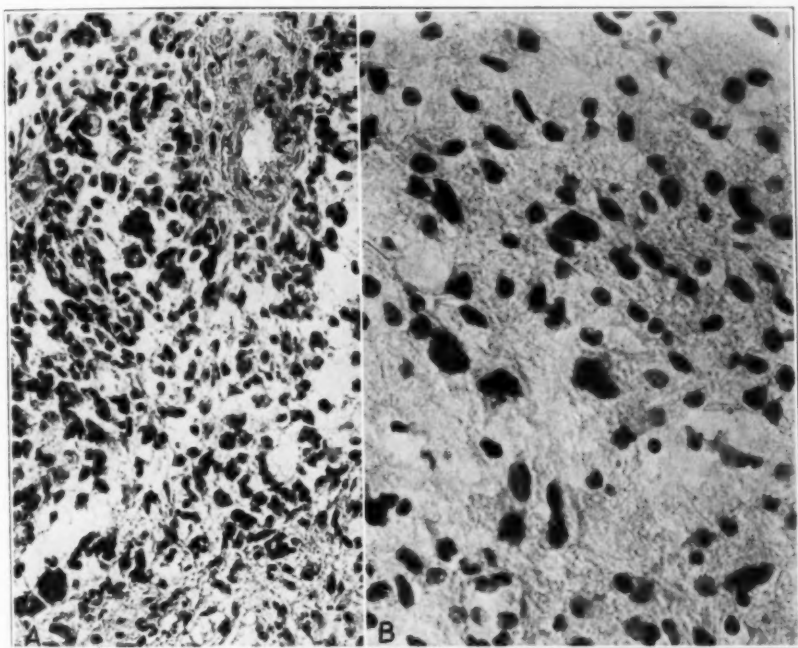


Fig. 7.—*A*, spongioblastoma multiforme. This is a characteristic section; giant cells, giant nuclei and many mitotic figures are present; some areas of necrosis and endothelial proliferation in the lumen of some of the vessels are present in other parts of this tumor (hematoxylin and eosin;  $\times 225$ ). *B*, spongioblastoma multiforme frequently referred to as giant-cell glioma of Stroebe. The variation in the nuclei is evident (hematoxylin and eosin;  $\times 375$ ).

cases tumors in parts resembled the tumor depicted by Penfield and Young. Most of the cells are not fully differentiated into astrocytes, such as are seen in the normal nervous system, but they more closely

8. Penfield, Wilder, and Young, A. W.: The Nature of Von Recklinghausen's Disease and the Tumors Associated with It, *Arch. Neurol. & Psychiat.* **23**:320 (Feb.) 1930.

resemble astroblasts. They have processes running to the perivascular spaces (fig. 6 *B*), but the cell bodies are small, and the cytoplasm is less abundant than in characteristic astroblasts of the cerebrum. Moreover, these tumors do not have multinucleated cells. Lateral small processes extend into the surrounding tissue for short distances. Except for the perivascular processes, the cells do not have any characteristic arrangement. Some regions are very cellular, but for the most part the tumors are composed of tortuous processes with few cells. The nuclei contain little chromatin, and mitotic figures are not seen. The patients from whom these tumors were taken gave histories of having had symptoms four and seven years prior to operation; they were living eight and seven years, respectively, after operation. Several pieces of tissue are available which were removed from the walls of cysts of the spinal cord. These contain many fibrous astrocytes, but the entire picture resembles that seen in the gliosis from the wall of a cavity in syringomyelia, so we do not include them as neoplasms.

#### OLIGODENDROGLIOMAS

Two tumors were encountered which in places had some of the appearance of the solid cell type of ependymoma, but in others the cellular arrangement around the blood vessels was atypical. The tumor cells do not have the definite eosin-staining cytoplasm. The nuclei are smaller, and instead of being surrounded by solid cytoplasm they are surrounded by clear spaces, which is characteristic of the oligodendrogliomas (fig. 8 *B*). This tissue had been fixed in formaldehyde several years before it was recognized as a possible oligodendroglioma; therefore, Hortega's specific stain could not be utilized. However, the general and cellular appearance strongly suggest oligodendroglioma, especially when comparison is made with the oligodendrogliomas reported by Bailey and Bucy<sup>9</sup> or with those arising in the brain in our own series of cerebral gliomas. Neither of these tumors is entirely typical. The atypical portion is not characteristic of ependymoma, for the nuclei are smaller and the cytoplasm is neither as distinct nor as abundant as in typical ependymoma. These two tumors are probably oligodendroglioma composed in part by fairly well differentiated oligodendroglia cells and in part by more embryonic oligodendroglia cells, or, as one might call them, oligodendroblasts. Some cells, more primitive than either of those just mentioned, are present in one of these neoplasms and are characterized by small, deeply staining hyperchromatic nuclei and scanty cytoplasm. In the midst of such a group of cells a few mitotic figures are seen.

9. Bailey, Percival, and Bucy, P. C.: Oligodendrogliomas of the Brain, *J. Path. & Bact.* **32**:735 (Oct.) 1929.

## MEDULLOBLASTOMAS

Medulloblastomas, except those in the cerebellum of children, are not common, although they have been described as occurring in the cerebrum, but they are not usually recognized as tumors of the spinal cord. In this group we have encountered four such tumors; the cells of three of these show a tendency to differentiate into spongioblasts, and the cells of one tumor show a tendency to differentiate into neuroblasts. This differentiation varies in different parts, even of the same tumor, but because medulloblasts are the predominant cells the tumors

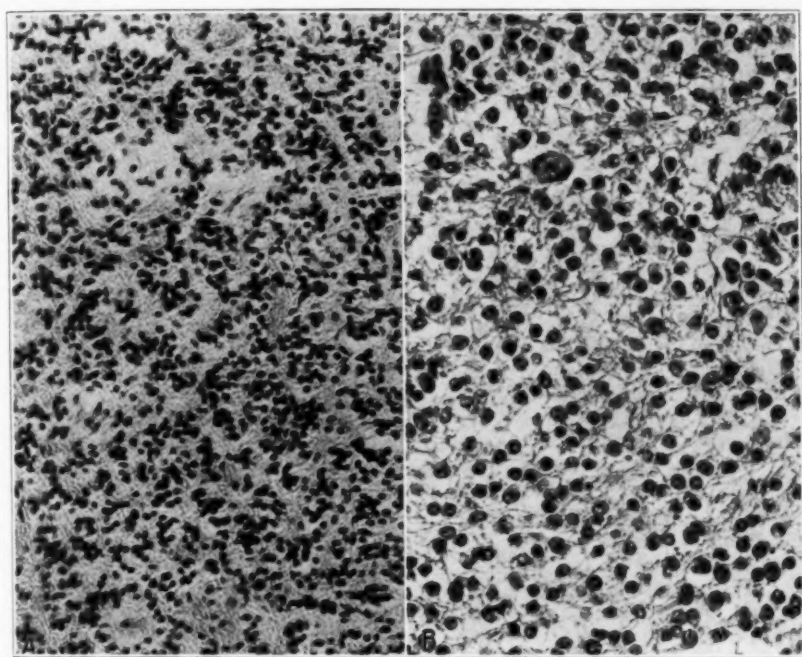


Fig. 8.—*A*, medulloblastoma. The cellular arrangement and cell type are characteristic (thionin;  $\times 200$ ). *B*, oligodendroglioma. This is a fairly characteristic picture, with small, deeply staining nuclei and the cell bodies appearing as vacuoles; little cytoplasm is seen (hematoxylin and eosin;  $\times 350$ ).

have been classified as medulloblastomas. Bailey and Cushing have shown that the medulloblastomas in the brain at times have this tendency to differentiate. The cells tend to arrange themselves in short rows; the nuclei are prominent, but the cytoplasm is small in amount and has a tendency to collect at one end in the shape of a short tail. The predominant cells are characteristic (fig. 8 *A*), but mitotic figures are much less common than in the same type of tumors of the cerebellum.

## GANGLIONEUROMAS

Neurogenic tumors are uncommon in the central nervous system, particularly in the spinal cord. In our series, there is one well differentiated ganglioneuroma, with masses of almost mature ganglion cells that are uniform, especially in their differentiation. They are characterized by the large vesicular nucleus and deeply staining nucleolus. The bodies are large, with immature Nissl granules, which stain blue with the thionin stain, and the chromatin is finely powdered. With silver impregnation (fig. 5 *A*) the bodies are seen to have from three to five or more dendrons, but axis cylinders are either not developed or fail to stain. In contrast to the ganglioneuromas that we have seen in the brain or in association with the sympathetic nervous system, binucleated or multinucleated cells are uncommon. The other tumor contains more primitive neuroblasts. The cells again have the characteristic, large vesicular nucleus and deeply staining nucleolus. The cells are in various stages of differentiation: bipolar, unipolar and multipolar forms are present in about equal numbers. There are no well differentiated forms, and no apolar cells are present. There are few cells with two or more nuclei. The silver stain does not help materially in demonstrating any processes. Some axis cylinders are visible but these seem to be inclusions from the adjacent normal spinal cord.

## HEMANGIOBLASTOMAS

In a recent contribution, Globus and Dorshay<sup>10</sup> reviewed the literature on intramedullary blood vessel tumors and found eight cases of hemangio-endothelioma; one of these tumors occurred in the cauda equina and probably arose from the filum terminale. In this series of cases we encountered four such tumors, which had characteristic histologic pictures. They are composed of dilated capillary spaces, and occasionally dilated larger vessels are encountered (fig. 9 *A*). In many of the capillary spaces the lining endothelial cells are swollen, and contain much lipid substance. Various stains show the reticulum forming the outline of the tortuous dilated capillaries. These four tumors show marked variation from the more solid, cellular type to the clear cell type. In one, very little lipid is present, the cellular cytoplasm stains with the cytoplasmic stains that are used as a routine, and some mitotic figures are encountered; in another, all the cells are filled with lipid substance and no mitotic figures are visible (fig. 9 *B*). In one case, in addition to two intramedullary hemangiomas (fig. 1 *B*), a cerebellar hemangioma and syringomyelia were present. Most cerebellar hemangioblastomas are accompanied by cysts, and in this case the cyst

10. Globus, J. H., and Dorshay, L. J.: Venous Dilatations and Other Intraspinal Vessel Alterations, Including True Angiomata, with Signs and Symptoms of Cord Compression, *Surg. Gynec. Obst.* **48**:345 (March) 1929.

may be represented by the cavity that is characteristic of syringomyelia. However, this was a typical instance of syringomyelia, with definite gliosis around the cavity, and was not an instance of hydromyelia; the central canal was represented by a small mass of ependymal cells lying between the syringomyelic cavity and the anterior fissure of the spinal cord. The upper tumor was not, in its entirety, a hemangioblastoma, but at its upper end the neoplasm was in part an ependymoma with tubules which were lined with typical ependymal cells. In this case, in addition to the hemangioblastomas of the spinal cord and cerebellum and the ependymoma of the spinal cord, there were multiple cysts of the

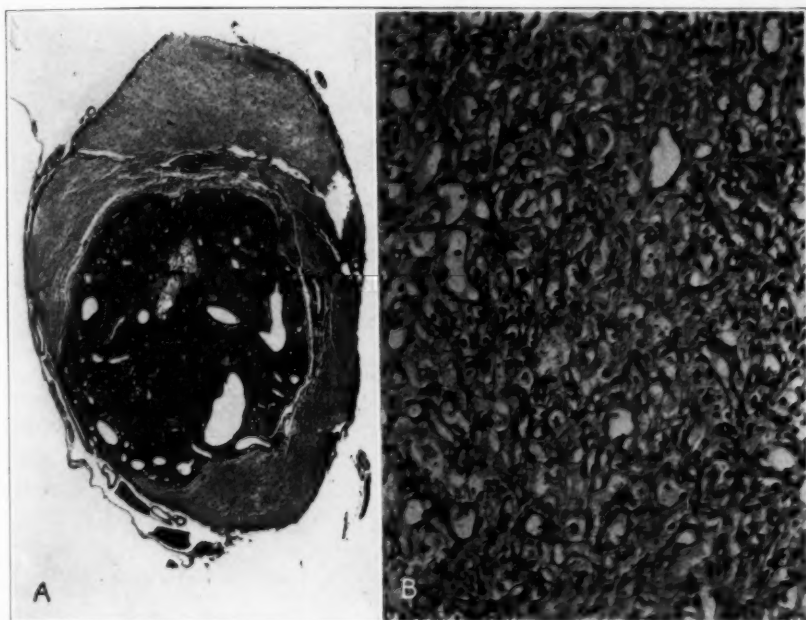


Fig. 9.—*A*, hemangioblastoma within the spinal cord showing compression of the cord and also impingement on the pia without invasion ( $\times 5.5$ ). *B*, hemangioblastoma composed of dilated capillaries. The lining endothelial cells in places are swollen and almost fill the lumen of the blood spaces (hematoxylin and eosin;  $\times 150$ ).

kidneys, the pancreas and the lungs and also multiple carcinoma of the kidneys, with metastasis to the omentum. In the other three cases it was impossible, at the time of operation, to determine definitely the presence of cavity or cyst formation in the cord.

#### FIBROBLASTOMA

Fibromas are unusual tumors to find in the substance of the spinal cord, but we have encountered one intramedullary tumor which must

be classified as a fibroma. The patient had a history of eight years of progressive symptoms from a lesion situated at the level of the fifth cervical segment of the spinal cord. At operation an intramedullary tumor was found and was partially enucleated. Histologic study showed the tumor to be a classic example of neurofibroma or perineural fibroblastoma. The cells are arranged in whorls, with interlacing fibrils, the nuclei are elongated and narrow and in places are arranged in palisades. Here and there, regions of the so-called foam cells and small regions of degeneration are present, with lymphocytic infiltration. Blood pigment is present in small amounts. It is impossible to classify this tumor in any other way than as a fibroma or a fibroblastoma.

#### LIPOMAS

Lipomas are occasionally encountered in the spinal cord, as is indicated by the work of Sachs and Fincher,<sup>11</sup> and by Stookey.<sup>12</sup> Approximately eight such tumors have been reported. In this series, one such tumor occurred in the cervical region of the spinal cord. The spinal cord was incised, and most of the tumor was removed, but it was not encapsulated as was the tumor reported by Sachs and Fincher. The gross and microscopic appearances of the tumor are characteristic, and the growth has the appearance of adipose tissue seen elsewhere in the body.

#### TUBERCULOMA

Elsberg,<sup>13</sup> in his book on tumors of the spinal cord, reported a tuberculoma as having arisen in the medullary substance of the spinal cord. We have encountered only one such tumor. The granuloma originated in the eighth cervical and first thoracic segments of the spinal cord and projected through its posterior surface. It was a large tumor, measuring 6 cm. in length and 2.5 cm. in diameter, so that there was much compression of the spinal cord. Grossly, the tumor resembled a lipoma and was thought to be that type of growth. However, microscopic examination showed it to be a classic tuberculoma. It is composed of conglomerate tubercles, with giant cells, and displays the fibroblastic reaction seen in some cases of the so-called hyperplastic type of tuberculosis. Little necrosis or cavitation is present. Subsequently, the patient died and necropsy was obtained, but there was no evidence of extensive tuberculosis either of the nervous system or of the body in

11. Sachs, Ernst, and Fincher, E. F., Jr.: Intramedullary Lipoma of the Spinal Cord, *Arch. Surg.* **17**:829 (Nov.) 1928.

12. Stookey, Byron: Intradural Spinal Lipoma, *Arch. Neurol. & Psychiat.* **18**:16 (July) 1927.

13. Elsberg, C. A.: *Tumors of the Spinal Cord*, New York, P. B. Hoeber, Inc., 1925, p. 421.

general. An excessive amount of fat is present in the tumor, giving it the appearance of a lipoma.

#### SYRINGOMYELIA ASSOCIATED WITH INTRAMEDULLARY TUMOR

Considerable interest has been shown in the association of syringomyelia and intramedullary tumor. This association has not been definitely demonstrated, nor has it been shown conclusively that there is no connection between these two conditions. It is not our object here to settle this discussion one way or the other, but some additional information and some more facts are offered for future consideration. In this series of intramedullary tumors of the spinal cord, necropsy was obtained in ten cases, in each of which the entire spinal cord was available for study. Some of the patients had not had previous operations.

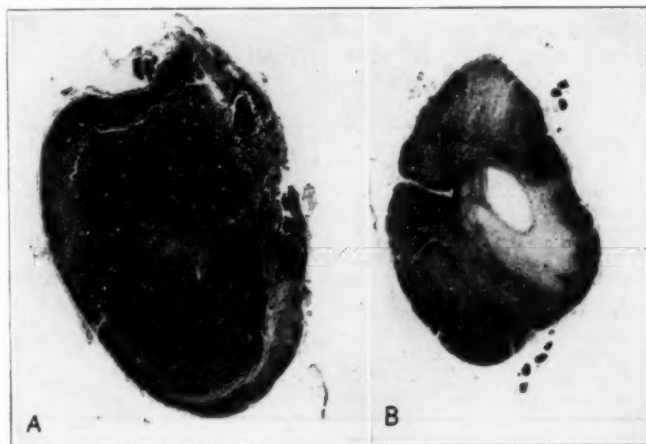


Fig. 10.—*A*, tumor within the substance of the spinal cord growing out into the subarachnoid space but not spreading around the spinal cord. There is extensive destruction of the substance of the cord (Weigert myelin sheath stain;  $\times 3.5$ ). *B*, syringomyelia in the same case as *A*, at a higher level.

In three cases necropsy was obtained elsewhere, and the spinal cords were sent to us for study; the patients had been seen and examined in the clinic previously. Of these ten cases of intramedullary tumor there was coexisting syringomyelia in five, and of the five in which syringomyelia was not present, one was a case of tuberculoma, which cannot be classified with the neoplasms, although the symptoms were those of such a tumor. Thus, of nine cases of neoplasm there was coexisting syringomyelia in five (55.5 per cent). Syringomyelia was not present in any of our cases of extramedullary tumor of the spinal cord. The five intramedullary neoplasms in which there was coexisting syringomyelia were as follows: hemangioblastoma (fig. 1 *B*), one; ependy-

moma (fig. 10 *A* and *B*), two, in both of which many canals lined with ependyma were present; medulloblastoma, one, and oligodendroglioma, one. It can thus be seen that syringomyelia does not accompany any special type of tumor. The syringomyelia in all these cases is characteristic. It is characterized by a cavity in the spinal medulla, extensive in its outline, and in one case extending as high as the nucleus of the eighth cranial nerve. The cavities are surrounded by gliosis, but this is not neoplastic, and the cavities are not lined with ependyma; the ependymal cells of the obliterated central canal lie between the syringomyelic cavity and the anterior fissure of the cord. Occasionally, cysts are described as coexisting with intramedullary neoplasms, but in our experience such cysts frequently prove to be syringomyelic cavities. In the nine cases of intramedullary neoplasms in which the spinal cords

*Duration of Symptoms of Intramedullary Tumors of the Spinal Cord  
(Prior to Operation)*

Type of Tumor	Years										
	1	2	3	4	5	6	7	8	9	10	10+
Ependymomas:											
Solid cell type.....	2	..	..	..	1	1	..	1	2	..	1
Tubular type.....	2	1	..	..	1	..	1	..	..	1	..
Neuro-epitheliomatous type.....	1	1	2	1	1	..	..	..	..	..	1
Spongioblastoma:											
Unipolare.....	1	..	..	..	..	..	1	..	..	..	..
Mixed.....	1	1	1	1	..	2	..	..	1	..	..
Multiforme.....	2	1	1	..	..	..	..	..	..	..	..
Astroblastomas.....	..	..	..	1	..	..	1	..	..	..	..
Medulloblastomas.....	1	..	..	1	1	..	..	1	..	..	..
Ganglioneuromas.....	..	..	1	..	1	..	..	..	..	..	..
Hemangioblastomas.....	2	..	1	..	1	..	..	..	..	..	..

were available for complete study, special interest was taken in subarachnoid invasion or extension of the tumor. In one case, numerous meningeal fibroblastomas, also perineural fibroblastomas, coexisted with an ependymoma, but in no case did the neoplastic cells extend along the subarachnoid space. Usually the neoplasm grows through the surface of the spinal cord and impinges on or occludes the subarachnoid space, but in no case was there any extension along this space to higher or lower levels, even in the case of the medulloblastoma.

#### COMMENT

There are several points in this series which are outstanding when the entire group is considered. The chief one is the duration of symptoms before operative relief was sought (table). The relatively long duration is remarkable when one considers the small diameter of the spinal cord and the slight injury which is required to lead to complete paralysis. The prolongation of the symptoms may in part be explained

on the basis that a small lesion produces symptoms, and consequently that symptoms appear earlier in cases in neoplasm of the spinal cord than in cases of neoplasm in any part of the brain, with the possible exception of the midbrain in the region of the aqueductus cerebri. It is difficult to explain why, in general, the duration of symptoms from tumors in which the cells are more completely differentiated is not longer than the duration of symptoms from tumors in which cells are less differentiated. There are exceptions to this statement. Patients with tumors of the type of spongioblastoma multiforme have much shorter histories than any other group, but the average duration of the history in cases of medulloblastoma is no shorter than that for the entire group. The only patients with tumors whose symptoms dated back ten years or more were those with ependymomas; of these there were three with histories of ten, thirteen and fourteen years, respectively. In one patient with an ependymoma of the lumbar portion of the spinal cord, the symptoms dated from 1912; the patient was operated on in 1921, and at present is entirely well. Most of the tumors in the group of gliomas are mixed, and few tumors are encountered that are composed of one type of glial or primitive glial cell. There are several tumors that contain cells of both neurogenic and spongioblastic nature. We encountered three gliomas that apparently originated in the subarachnoid space. The presence of these neoplasms in such a situation could be explained only by assuming that the source of the tumors was the spinal medulla, and that the tumors had grown out by pedicles which had disappeared or were unrecognized, or else that the tumors had originated from the heterotopic masses of glia or ependyma that we have encountered repeatedly in the subarachnoid space.

Little can be added concerning the association of syringomyelia and intramedullary tumor, except to point out that the association seems to be too frequent to be accounted for as a mere coincidence. Five cases of syringomyelia were found in association with nine cases (55 per cent) of intramedullary neoplasm. In one case there was a region in the posterior column in which the glia was arranged as in syringomyelia, but at the time of examination complete lysis had not occurred, although undoubtedly it would have occurred shortly. However, as there was no cavitation, this case has not been classified as an instance of syringomyelia. The type of tumor does not appear to have any bearing on the formation of cavities within the spinal cord.

We have divided the ependymomas into three groups, entirely on a histologic basis. This seems to be justified, since the arrangement of the cells in each of these groups is different and characteristic. However, such classification is not justified from the clinical or surgical point of view. In these groups there were cases with symptoms ten

years or longer in duration, but there were also cases in which the symptoms had been present one year or less, so that there is wide variation, as can be seen from the table. Each of these three types has been described previously by various authors, and their differentiation is accepted without question, except, perhaps, their identification of the neuro-epitheliomatous type. In this type the rings of ependymal cells surrounding a myxomatous mass usually are associated with the solid cell type of ependymoma, and occasionally these rings are found in a tumor with canals lined by ependyma. To us, this tumor is as much an ependymoma as either of the other types, and as such should be included in the group of ependymomas. This is the only type of tumor in which mucus is present in any appreciable amount. The spongioblastomas are more difficult to classify. The unipolar spongioblasts offer no difficulty, for they are characteristic, and the group of spongioblastoma multiforme can also be classified without much difficulty. Globus and Strauss, in their original paper on spongioblastoma multiforme, described for the first time such a neoplasm in the spinal cord, but subsequent contributors have failed to take advantage of their suggestion. It is in the group called simply spongioblastomas that difficulty is encountered, and more work is necessary on this group before they will finally be allocated their proper place. The difficulties arise from the fact that this entire group is made up of mixed cells. Spongioblasts predominate, but various types of spongioblasts are present, as well as occasional neuroblasts, and sometimes even small groups of medulloblasts. The seven cases included under this heading are all different in the distribution of the cell type, and it is impossible to deal with each one in this paper. Therefore, the simple term spongioblastoma represents a very mixed type of tumor.

The cellular characteristics of tumors with more completely differentiated cells, namely, the astroblastomas, astrocytomas and oligodendrogliomas, are fairly uniform within their respective classes, but the cellular character of the less differentiated group, the medulloblastomas, is less typical. This is because they show a tendency to become more completely differentiated. The medulloblast is a bipotential cell, and in its differentiation it may produce either a spongioblast or a neuroblast. In the four cases described by us, this tendency was well illustrated, and occasionally in the same tumor in which medulloblasts predominated, spongioblasts or neuroblasts were seen to exist. In one tumor all three types of cells coexisted, the medulloblasts being the more numerous.

Two tumors are described as ganglioneuromas. In reality, one tumor is a well differentiated ganglioneuroma with cells of typical uniform appearance and distribution. Although almost all the cells of the other tumor are at the same stage of differentiation and are in the same characteristic distribution, they are more primitive, and the tumor should

really be classified as a neuroblastoma unipolare; nevertheless, occasional bipolar and multipolar neuroblasts are present. Tumors of neurogenic origin are rare in any part of the nervous system, particularly in the spinal cord. We have been unable to find any other reports of cases of neurogenic tumors of the spinal cord.

Little need be said of the hemangioblastomas, except that their cells, like those of some of the gliomas, vary in their degree of differentiation. One tumor of this group of hemangioblastomas was much more malignant than any of the others, and mitotic figures were seen. It recalled the appearance of a sarcoma vividly in spite of the fact that it was a characteristic hemangioblastoma. It is impossible to explain the presence of the fibroma in the middle of the spinal cord, especially as this tumor had the characteristic appearance of fibroblastoma of the acoustic nerve. The silver stain failed to reveal axis cylinders in this tumor which had the whorls, palisade arrangement, delicate elongated nuclei, foam cells and granules of blood pigment characteristic of tumors of the acoustic nerve.

The small number of tumors in many of the subgroups of the intramedullary tumors of the spinal cord may prove this attempted classification unjustified, but the classification demonstrates that in the spinal cord occur glial tumors of most of the types found in the brain. It may also stimulate further work and contributions, so that ultimately a more thorough understanding of these tumors may be obtained, and a more hopeful view of the prognosis reached.

#### ABSTRACT OF DISCUSSION

DR. PERCIVAL BAILEY, Chicago: I am delighted to see that the structure of gliomas of the spinal cord parallels the structure of gliomas in the brain.

I agree with practically all the diagnoses that Dr. Kernohan has made except perhaps two, and if I saw the original preparations I might agree with those, but judging from the photographs that were shown, I might be inclined to question the diagnosis of the neuro-epitheliomatous type of ependymoma. I think that those cavities are not vesicles but blood vessels in every case. I have seen two such tumors and have made the same interpretations to begin with, but have finally convinced myself that those are blood vessels and that the papillomatous appearance is due to degeneration between the blood vessels. As I say, that may be an erroneous interpretation, and Dr. Kernohan may be right. I would not want to judge finally until I saw the original preparation.

I have had little experience with these spinal tumors myself because in Dr. Cushing's clinic they were rather rare, and I have not had much occasion to examine them. I think that it would be an excellent idea if we could establish a central registry for these gliomas of the spinal cord such as has been established for sarcoma of the bones, for instance, because they are so rare in any one's experience that it will be exceedingly difficult for any one to have as much experience again as Dr. Kernohan has had, at least within a period of a great many years.

DR. WILDER G. PENFIELD, Montreal, Canada: It is only by such large collections of tumors of the spinal cord that one can begin to get an idea of these tumors, and it is a real service that Dr. Kernohan has performed. I would like to bring up the question of one group of tumors, the spongioblastomas of the mixed type. Dr. Kernohan speaks of the spongioblastoma multiforme, which is, of course, quite a definite entity. Then he speaks of the unipolar spongioblastoma which is an entity also, made up of polar cells and perhaps better called polar spongioblastoma, but the mixed spongioblastoma is not a histologic entity. Any spongioblastoma that contains neuroblasts, as he pointed out, has no right to be called a spongioblastoma. Would it not be better under the circumstances to group such tumors under the heading of glioma, type undetermined, until their type has been worked out?

It seems to me that, for the diagnosis of spongioblastoma multiforme, we must demand the typical change of blood vessels which these tumors show, and is more characteristic of them than any cell type, namely, the outbudding of tissue from the small vessels in the tumor. This vascular change seems even to precede the advance of the tumor through the brain.

DR. WILLIAM G. SPILLER, Philadelphia: One must be deeply impressed by the extraordinary number of cases of intramedullary tumors reported in this paper. It is somewhat remarkable also that the intramedullary tumor has a considerably longer duration than the extramedullary and the extradural tumors. At first, one would suppose that the intramedullary tumor destroys more tissue and destroys it more rapidly than a tumor which has space to develop in the extramedullary or the extradural region. I think that if these tissues had been studied by Bielschowsky's silver stain, one might find that in many of these tumors axis cylinders passed directly through the tumor without being destroyed, and therefore were capable of functioning, although under difficulty.

Some years ago, being impressed with the fact that large gliomas of the brain often were present when the symptoms gave comparatively little indication of the intensity of the process, I suggested to Dr. Byrnes of Baltimore, who was working in my laboratory, that it would be well for him to stain the tissue immediately below, above and within such a glioma by the silver stain, and he was able to show the existence of many axis cylinders which previously by other methods had not been detected.

I note also that the authors of this paper say that they are uncertain in their diagnosis of intramedullary and extramedullary tumors. That has been my own experience. I have concluded that a sure diagnosis whether the tumor is within the cord or is extramedullary is often an impossible diagnosis to make. A guess may, of course, be made.

I conclude from the statements that have been made by the authors that operation on these intramedullary tumors in their hands has been successful and that they advise operation on such tumors.

DR. JOSEPH H. GLOBUS, New York: I should like to say a word of approval of this excellent piece of work which has filled a large gap in our knowledge of tumors of the central nervous system. Here is the first attempt to place the classification of tumors of the spinal cord on a sound basis. It is, of course, an important contribution. One should hesitate to add a single word of doubt, based on a minor point of disagreement, since it may distract from the excellence of the work.

DR. KERNOHAN: The ependymomas, which I have called the neuro-epitheliomatous type, have been so designated because in some respects they simulate

a neuro-epithelioma. The centers of the spaces were filled with mucus and did not contain blood vessels. However, blood vessels may have been there previously. In the other parts, the tumor was undoubtedly ependymomatous.

As I have already stated, there was some doubt in my mind about the mixed type of spongioblastomas. This term was suggested because the majority of the cells were spongioblasts. In two of them I did find neuroblasts, but such cells were rare. I doubt if they all fit in with Dr. Bailey's suggestion that they are protoplasmic astrocytomas; more tissue and special stains will be necessary before this point can be settled definitely. This group of tumors varies greatly in appearance, and in consequence they should be dealt with individually rather than as a group. Perhaps Dr. Penfield's suggestion that they should be left as unclassified gliomas is the best solution of the problem for the moment.

In this group of tumors, axis cylinder stains were done whenever possible. It was unusual to find axis cylinders in the neoplasm; usually the tumor had pushed aside the fibers rather than surrounding and including them in its progress. Occasionally, axis cylinders were included in the progress of the neoplasm but this was the exception rather than the rule.

## THE CEREBELLUM

COMPARISON OF SYMPTOMS RESULTING FROM LESIONS OF INDIVIDUAL LOBES WITH REACTIONS OF THE SAME LOBES TO STIMULATION: A PRELIMINARY REPORT \*

AUBREY T. MUSSEN, M.D.

BALTIMORE

In previous papers describing the response of the cerebellar cortex to the faradic current, it has been claimed that the individual lobes showed localized reactions. Thus, in the vermis when the anterior lobe was stimulated the posterior muscles of the neck contracted; when the posterior lobe was excited, the response was in the anterior muscles of the neck, and the middle lobe of the vermis rotated the head and eyes toward the side that was irritated. In the hemisphere the middle lobe was concerned with lateral flexion of the head, while the posterior lobe was in relation with the back and the extremities—the paramedian lobe with the fore leg, the paraflocculus anterior with the hind leg and tail, the posterior region with the fore leg and the median region with the back. The ventral lobes, the uvula, the nodule and the lingula are associated with the lips, tongue, throat, larynx and pharynx.<sup>1</sup>

As such a view of cerebellar localization differed entirely from the opinions of all other investigators, it has naturally received much adverse criticism, and the only answer that in the past could be given was: (1) that these localized reactions were found in the cat, rabbit and monkey, and (2) that corresponding lobes in these different animals gave similar responses. Usually such corroborative evidence would have been sufficient by itself, but the fact that practically every investigator has failed in attempts to show that the cerebellar cortex gave localized

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\* Read at the Fifty-Sixth Annual Meeting of the American Neurological Association, Atlantic City, N. J., June 10, 1930.

1. Mussen, A. T.: Experimental Investigations on the Cerebellum, *Brain* **50**:313, 1927; The Cerebellum, the Method of Stimulation and the Influence of Localized Lesions, *J. Nerv. & Ment. Dis.* **71**:185, 1930; The Cerebellum: A New Classification of the Lobes Based on Their Reactions to Stimulation, *Arch. Neurol. & Psychiat.* **23**:411 (March) 1930.

responses on stimulation made it compulsory to prove conclusively that the reported reactions actually did exist.

It occurred to me, therefore, that the most positive evidence that could be advanced to support the claim that the cerebellar lobes have individual functions would be to demonstrate by localized destruction of the lobes that the resulting symptoms agreed in principle with the reactions obtained in the same lobes by electric stimulation. That is, that if the anterior vermis on stimulation produced contractions in the posterior muscles of the neck, a lesion in the anterior vermis, by dissociating the activity of these muscles, would allow the anterior group of muscles of the neck to act without opposition, with the result that the maintenance of forward balance would be interfered with. The same argument would apply to the posterior vermis. If this lobe, which stimulation shows controls the activity of the anterior muscles of the neck, was destroyed, the posterior muscles of the neck under the control of the anterior vermis would react too strongly and backward balance would be disturbed.

Up to the present, lesions have been made in the anterior, posterior and middle lobes of the vermis and in the lobus paramedianus of the posterior lobe of the hemisphere. In making these lesions, several methods were tried.

#### METHODS

1. The lobe to be destroyed was freely exposed, and each folium was cauterized to a depth of about 5 mm. The disadvantage of this procedure was that serious hemorrhage from the porous bone often resulted and interfered greatly with the usual quick recovery, so that it not infrequently happened that owing to general weakness it was impossible to make any examination for several days. And as the incoordination produced by the lesion is of particular interest during the first few days, before any readjustment takes place, this most usual method is not to be recommended. The cautery itself is also a source of danger as the destruction that follows its use is usually much greater than was intended.

2. Another method was to expose the lobe and insert the cutting needle of the stereotaxic instrument through a puncture in the dura, and then make a subcortical lesion in each folium. While this is an improvement on the preceding method in that the dura is not opened and the lesion is better localized, it still has the disadvantage of the preliminary exposure and accompanying hemorrhage.

3. The procedure that gave the best results was to expose the bone and trephine with a 5 mm. drill, and through this opening to insert the cyclotome of the stereotaxic instrument, to a point that had been previously determined on the chart, and to cut the main stem of the arbor vitae to the lobe under consideration. As all afferent and efferent impulses would thus be interrupted, the effect would be the same as if the cortex of the lobe had been destroyed. Or instead of this, subcortical lesions could be made. This method has a tremendous advantage over all others as there is no hemorrhage, consequently no shock, and as the disturbance to the cerebellum is reduced to a minimum the early symptoms are more readily observed.

## RESULTS

*The Posterior Vermis.*—If it is true that stimulation of the lobus pyramis by acting on the anterior muscles of the neck flexes the head forward, which suggests that this lobe is concerned with the regulation of backward balance, it should follow that destruction of the lobe by allowing an overaction of the unopposed posterior muscles of the neck would produce such a disturbance in equilibrium that the mechanism of backward balance would be interfered with.

In experiment 303, the main branch of the arbor vitae to the lobus pyramis of a cat was cut by insertion of the cyclotome through a 5 mm. drilled open-

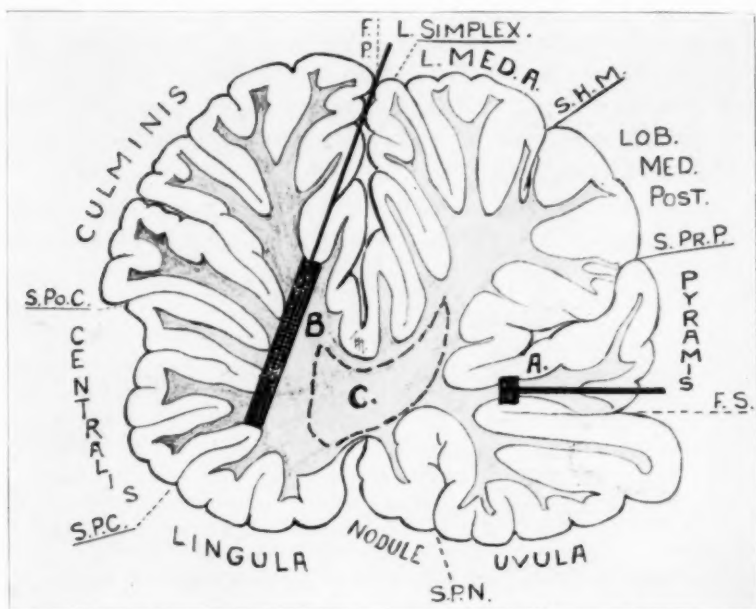


Fig. 1.—Median sagittal section of the cat's cerebellum, showing: *A*, lesion of the main trunk of the arbor vitae to the lobus pyramis, and the path of the needle; *B*, lesion of the arbor vitae of the centralis and culminis; *C*, comparative size and position of the roof nucleus a few millimeters lateral to the median line.

ing in the occipital bone. The cerebellum was not exposed and no other lobe was interfered with. By this method all the afferent and efferent fibers to and from the lobe were interrupted, and the same effect was produced as though the cortex of the whole lobe had been destroyed (fig. 1*A*).

On the following day, the animal appeared to have fully recovered. When placed free on the floor, it ran quickly forward and bumped into the leg of the table and a chair. The righting reflexes were much more active than normal, and when held erect and suddenly let go, the cat fell backward. On jumping from a chair there was no tendency to fall forward, though after landing it swayed forward and backward. During the following week, the irritative symp-



Fig. 2.—Lesion in the posterior vermis, as illustrated in figure 1*A*. *A* shows loss of backward balance; *B*, that the forward balance in the same animal is normal. See text for description.

toms gradually disappeared. The righting reflexes became more normal, the sudden running and bumping into things was less noticeable and there was very little oscillation when standing still. When held erect and suddenly let go, the falling backward was very marked. There was no evidence that forward equilibrium was disturbed. Motion pictures taken on the ninth day illustrate the character of the test and the loss of backward equilibrium, while in jumping from a chair the action is normal. This loss of backward balance persisted to the twenty-first day, when the animal was chloroformed and the brain removed for examination by the Marchi method.

In examining a cat with a lesion in the lobus pyramis of the posterior vermis several different tests were made: One was to hold the animal in a standing position with hind and fore feet against the wall. If the whole of the lobus pyramis had been destroyed, the animal, when suddenly let go, would fall directly backward. Another test was to observe the manner in which it attempted to jump up on a chair. It was then seen that though the effort to jump was made it was not properly coordinated; the cat jumped too high and too straight upward and, failing to reach its objective, fell over backward. While both of these tests showed that backward balance had been disturbed, it was difficult to interpret just what happened. The test that gave the most information was to hold the cat in the erect position with its hind feet on the floor and slowly pull it backward. It then became immediately apparent that some disturbance in equilibrium was present, for the animal allowed itself to lean backward resting in the investigator's hands, with legs relaxed and dragging, so that when suddenly let go it naturally fell backward. That the lesion involves backward balance alone was shown by the ability of this animal to jump from a chair to the floor without any indication that forward equilibrium was disturbed.

This experiment shows clearly that the lobus pyramis is primarily concerned with the maintenance of backward balance through its influence over the anterior muscles of the neck, and if the lobe is destroyed that backward balance is lost; it proves also that the reactions obtained by stimulating the lobe were a correct indication of its function.

*The Anterior Vermis.*—The function of this region of the cerebellum, as shown by stimulation experiments, is to contract the posterior muscles of the neck and pull the head backward. From this it was argued that the center for maintaining forward balance was located in these anterior lobes; consequently, if these lobes were destroyed, the ability to preserve forward balance would be lost.

In experiment 300, the position of the arbor vitae of the lobus centralis and culminis was located on the chart and the point of entrance determined. Through a 5 mm. trephine over the culminis the cyclotome was inserted with the aid of the stereotaxic instrument, and the fiber arms of these lobes were cut. No other lobes were interfered with (fig. 1B).

On the following day, though the animal had not sufficiently recovered to be removed from the basket, it showed an increase of tone in the anterior muscles of the neck, with flexion of the fore limbs and stiffness of the hind limbs. On the second day, when placed on the floor the gait was seen to be very ataxic. The head was held low, the body in a crouching position with the fore legs more flexed than the hind legs. On the third day, it was able to walk more steadily. The

tone in the anterior muscles of the neck was distinctly increased, as it was more difficult to bend the head backward than forward. In the fore limbs the tone was diminished and the hind legs showed a very active knee jerk. When held by the shoulders and drawn backward, a normal equilibrium was maintained; there was no suggestion of falling. But when the forward balance was tested by making it jump from a chair there was a very evident disturbance, for equilibrium was entirely lost, and on landing the animal fell over on its head. Motion pictures were taken showing the lost forward balance (fig. 3).

This experiment also proves that the stimulation reactions were correct; that the anterior vermis is concerned with the regulation of forward balance through its influence over the posterior muscles of the neck, and if the lobes of the anterior vermis are destroyed, that the anterior muscles of the neck under the control of the posterior vermis and acting without opposition, will cause such a disturbance in equilibrium that forward balance will not be preserved.

*The Middle Lobe of the Vermis.*—This lobe is made up of the lobus simplex, the lobus medianus anterior and the lobus medianus posterior. It is particularly with the latter that I am concerned for it is the folia of this lobe, which in the cat are frequently arranged in the form of an "S" laid transversely, that have given such definite rotation movements of the head, accompanied by conjugate deviation of the eyes toward the side stimulated. It was considered, therefore, that if the folia forming the left half of this lobe were destroyed, the balancing reactions of the two halves of the lobe would be interfered with, and the normal right half acting unopposed would turn the head and eyes to the right.

In experiment 312, the lobus medius posterior was exposed, and when the unusually severe hemorrhage had been controlled, a clear view of the four folia which in this animal formed its left half was obtained<sup>1a</sup> (fig. 2). After protecting the surrounding lobes with wet cotton, each folium was punctured twice with the cautery. The dura was then replaced and the wound closed.

On the following day, although the cat was too weak to permit a thorough examination, it was noted that the head was strongly turned toward the right, and the eyes showed vertical nystagmus both when lying down and when in the erect posture. When held up by the back, the head and body were curved to the right, and on being returned to the basket there was a strong spasm in the muscles of the neck, the head being drawn backward and to the right (fig. 4).

On the second day, the condition being somewhat improved, motion pictures were taken showing the head strongly flexed to the right, the nose resting in the hollow of the right flank. This position was maintained throughout the exposure.

Here again the correctness of the stimulation reactions are confirmed by the symptoms produced by this localized lesion.

*The Lobus Paramedianus.*—This is one of the lobes forming the posterior group of the hemisphere. In the cat it is composed of three lobules which the stimulation reactions have shown to be related to the

1a. Mussen (footnote 1, third reference, p. 432, fig. 2).



Fig. 3



Fig. 4



Fig. 5

Fig. 3.—Lesion in the anterior vermis, as indicated in figure 1B, showing cat jumping from ledge, losing its balance and falling over forward on its head. The backward balance was not disturbed.

Fig. 4.—Lesion of the left half of the lobus medius posterior of the middle lobe of the vermis, showing the reaction of the unopposed normal half in turning the head to the right.

Fig. 5.—Lesion of the dorsal lobule of the right lobus paramedianus, illustrating the ataxia in the right fore leg, which is shown to be lifted too high and extended too far forward.

movements of the fore leg on the same side. The dorsal lobule is concerned with the movements of the shoulder, the middle lobule with the musculature of the upper leg and the ventral lobule with the activities of the foreleg and the paw. When the folia which form the dorsal lobule were tested with the faradic current, it was found that while the reactions were limited to the shoulder, they were of various kinds: elevation, forward and backward movements, and combinations of these. As all of these activities are to be found within the very small area of these dorsal folia, it was impossible to tell what the exact result of a lesion would be, but it was expected that whatever symptoms were produced would be confined to the shoulder.

In experiment 297, the folia forming the dorsal lobule of the right lobe were clearly exposed and then cauterized<sup>1a</sup> (I.C. p. 22). Unfortunately, there was considerable hemorrhage, which left the animal in a weakened condition for a few days (fig. 5).

Examination on the third day showed the following symptoms: When placed on the floor, the animal at first turned in circles to the left. In walking and running there was staggering to the left, accompanied by ataxia in the right fore leg which was raised too high, thrown too far forward and brought down too suddenly. It is of interest to note that a trial experiment in the previous year showed exactly the same symptoms. The tests for balance and the righting reflexes were not satisfactory on account of the condition of the animal. Motion pictures showing the incoordination in the movements of the shoulder were taken. Infection developed and the animal was chloroformed on the sixth day.

#### COMMENTS

This preliminary research on the effect of localized lesions of the cerebellum proves conclusively that the stimulation reactions did correctly indicate the function of the individual lobes operated on. And the question that now naturally arises is, Do these experiments throw any light on the nature of cerebellar activity?

Since Sherrington<sup>2</sup> drew attention to the head as the most important segment of the body on account of its association with posture, more particular interest has been directed to the investigation of this relationship. It has gradually become recognized that voluntary control of equilibrium is influenced by the various afferent impressions derived from sight, the vestibular and auditory apparatus and the sensations from the skin, muscles and joints. Then Magnus,<sup>3</sup> as a result of his experiments on decerebrate and thalamus animals, was able to show that the effect of passively moving the head was transmitted to the muscles of the neck, and through them the tone in the limbs was altered, and a definite relationship was established between the neck reflexes and both static and kinetic postures.

2. Sherrington, Charles S.: *The Integrative Action of the Nervous System*, New Haven, Conn., Yale University Press, 1906.

3. Magnus, R.: *Körperstellung*, Berlin, Julius Springer, 1924.

But the central organization which, in an intact animal, is responsible for coordinating the various afferent impulses that are necessary for every activity, including the righting reflexes and the preservation of posture, had not as yet been determined. Magnus considered that the red nucleus was the coordinating center, for in his experiments when the cerebellum was removed the postural reflexes were not in any way affected. Evans<sup>4</sup> expressed the view that this fundamental function of coordination is situated in the cervical cord, and even went so far as to say that in the simple readjustment of posture it seems certain that the cerebellum is not concerned.

It is directly in connection with this question of the central control of the various afferent impressions, the coordination of which is necessary for all activity, including equilibrium, that the results of these researches offer some interesting facts which suggest a new interpretation of cerebellar function.

It is, I believe, generally admitted that the fundamental function of the cerebellum is synergia, which is defined as the power by which movements more or less complex but functionally definite are associated in special acts.<sup>5</sup> The movements to which reference is generally directed are those of the limbs, the musculature of which is described as being composed of unit groups containing both agonists and antagonists. But there are other important groups of muscles not usually considered in this connection, viz., the muscles of the neck, for it is by these that the movements of the head are controlled, and through them that the activities in the limbs and trunk are coordinated.

The muscles of the neck, like those of the limbs, are also arranged in groups containing agonists and antagonists, representing synergic units. There is an anterior group opposed by a posterior group, the function of which is to regulate forward and backward balance; there is a left central opposed by a right central group concerned with the rotation movements of the head, and in the hemisphere there is an anterolateral opposed by a posterolateral group, a left lateral and a right lateral group, connected with the lateral movements.

The particular knowledge of the relation of these various groups of neck muscles to the cerebellar lobes, gained in three years by stimulation experiments on the cat, rabbit and monkey, and the opportunity for the repeated examination of animals with known localized lesions of the cerebellum which principally affected these muscles, has helped greatly in understanding the symptoms observed. Such an analysis

4. Evans, C. Lovett: *Recent Advances in Physiology*, London, University College, p. 305.

5. Mills, C. K., and Weisenburg, T. H.: *Cerebellar Symptoms and Cerebellar Localization*, *J. A. M. A.* **63**:1813 (Nov. 21) 1914.

suggests that the function of the cerebellum may be brought into play in two ways: either through the primary disturbance of equilibrium, the limbs being secondarily involved, or with a limb primarily affected, the adjustment in equilibrium being secondary. In other words, the primary cerebellar activity depends on the particular lobe or lobes first involved, and the secondary response is made up of the integrative synergic activity set in motion by the primary reflex.

I shall apply this theory to the experiments that have just been presented in which the lesions were known and the symptoms limited.

*Anterior and Posterior Vermis.*—To appreciate the importance of the synergic units which form the musculature of the neck, I shall first consider the results obtained from the experiments on decerebrate animals in which the voluntary control of posture had been eliminated, for these are of particular interest when the reactions of a normal animal are compared with those of one in which there has been a localized cerebellar lesion. In the decerebrate specimen it has been shown that when the head is bent forward the tone in the fore limbs is diminished while that in the hind limbs is increased, and when the head is bent backward the reverse takes place, the fore limbs being extended and the hind limbs flexed.

Now if one observes an intact animal in the act of jumping from a table to the floor, it will be noticed that the accuracy of the movement is entirely dependent on the normal functioning of the anterior and posterior reflexes of the neck. The act, which is first decided by voluntary control, is then prepared for by the coordination of the various impulses which are received through the visual and vestibular apparatus as well as the sensations from the limbs. As a result, the head is fixed in a forwardly flexed position, the tone in the fore limbs is somewhat lessened, and that in the hind limbs is increased. Then as soon as the spring is made and the animal begins to fall, a change in posture is noticed, for it is necessary first that the center of gravity must be maintained posterior to the shoulders if a four point landing is to be accomplished, and second, the proper preparation for landing has to be provided for. Owing to the normal coordination of the anterior and posterior muscles of the neck, the tone in the latter is gradually increased and the head is drawn backward so that the center of gravity of the body in space is properly maintained. Then in preparation for landing there is a further retraction of the head followed by an increase in the extension of the fore limbs, while the tone in the hind limbs is decreased.

In a normal animal it is therefore clearly demonstrable that the act of jumping from a table is dependent on two definite cerebellar activities: (1) the primary reflexes of the neck, which are constantly changing under the influence of the alternating afferent impressions, and

(2) the secondary response in the general musculature of the limbs and trunk, which provides that the center of gravity is correctly maintained so that the proper performance of the act is assured. The interest of this analysis lies in the fact that in animals with lesions in the anterior or posterior vermis entirely different results are to be observed.

When a cat with the centralis and culminis of the anterior vermis destroyed is placed on a table and an attempt is made to make it jump, several interesting facts are to be noted. As it still has voluntary control of its movements, it realizes that something is wrong and protests. If pushed off it will cling with its fore paws and fall sideways. When again gently persuaded, if proper direction is maintained,

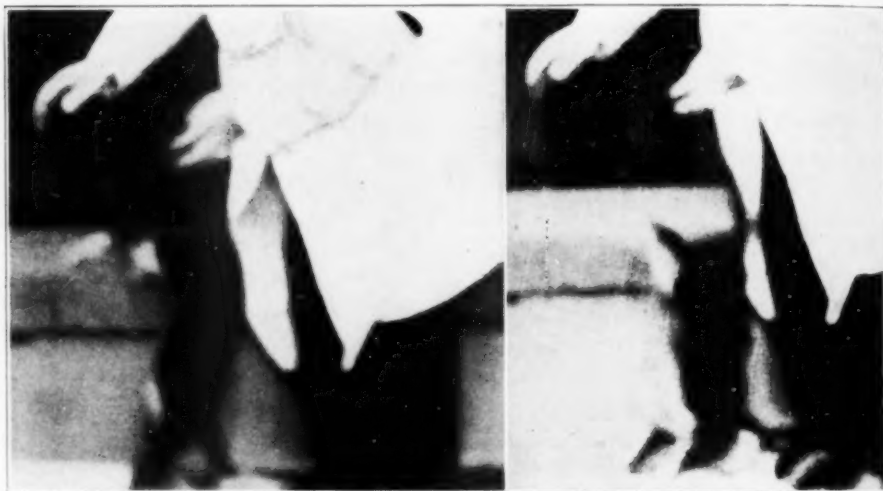


Fig. 6.—The effect of a lesion in the anterior vermis with loss of forward balance. The position is too perpendicular, the center of gravity is too far forward and equilibrium is entirely lost. In addition to this, although the head is somewhat retracted, the fore legs are under the body instead of being forward. When landing in such a position, the animal must overbalance. Compare with a cat making a normal forward jump, as in figure 2B.

it will go off head first; but it will be noticed that the head is held too low and the animal crouches too much on its fore legs, the tone of which is too much diminished, while the tone in the hind legs is too much increased. The consequence is that a proper take-off is impossible, as the effort of the fore legs is not sufficient to throw the body far enough forward to assure a proper equilibrium, and the animal slips over the edge of the table. Then as the tone in the hind legs is too much increased, owing to the unopposed activity of the anterior muscles of the neck, too much of a spring is made and the hind quarters are

thrown too far outward so that the animal begins its descent almost perpendicularly. During the fall, as the visual and vestibular impressions cannot be coordinated owing to the lesion in the anterior vermis, there is no attempt to reestablish a normal center of gravity, and as it is impossible for the posterior neck reflexes to be developed, the head is not retracted sufficiently nor the fore legs far enough extended, so that when the animal lands on its fore feet, in a perpendicular position, with equilibrium entirely lost, it falls on its head and rolls over on its back (fig. 6). The animal in figure 6 showed no disturbance in backward balance.

In this instance, the manner in which the cerebellum acted is clear. As the lesion involved the anterior vermis the posterior muscles of the neck were thrown out of coordination, and the anterior muscles of the neck acting unopposed produced the first evidence of the disturbance, viz., the primary anterior neck reflex. The secondary response then developed, and the limbs and body were brought into proper relation with the position of the head. But as the primary neck reflex was wrong for this particular act, the center of gravity was thrown too far forward, and as no readjustment in equilibrium could take place, the balance was completely lost, and the animal fell over on its head.

In the explanation of the loss of backward balance when the posterior vermis is destroyed, the same argument is applicable. In order to appreciate why the lobus pyramis, which normally is responsible for the maintenance of backward balance, will cause the animal to fall backward when destroyed, one may observe how a normal cat behaves when examined under similar conditions.

If a normal cat is held by the shoulders with its hind feet on the floor, and then is petted a little until the tension of being handled is relaxed, it will be found possible to hold it in a perpendicular position with the head almost erect and the tone in the hind limbs lessened. But as soon as one begins to pull it backward, there is an immediate alteration in posture. The threatened loss of equilibrium gives rise to impulses from the vestibular apparatus, from vision and from the changed position in the body and limbs which on reaching the posterior vermis are coordinated. The first indication of cerebellar activity to this threatened loss of forward balance is the primary anterior neck reflex, which bends the head well forward and gives rise to the secondary response which increases the tone in the hind limbs. Associated with this there is a quick stepping backward in order that the body may be brought into a forwardly inclined position, so that, with the center of gravity normally established, its equilibrium is regained, and when suddenly let go it drops into a sitting position (fig. 7).

But a cat with a lesion in the posterior vermis, tested in the same manner, gives an entirely different reaction. When held quietly by



Fig. 7.—Normal cat being pulled backward. Note the anterior neck reflex, body with the center of gravity well forward. The great increase in the anterior relaxed fore legs, increased tone in the hind legs and tail and the position of the neck reflex is shown, with tense hind legs and tail, and how by stepping backward the center of gravity is thrown forward and equilibrium is regained.

the shoulders with the hind feet on the floor, the head will be observed to be well up or somewhat retracted, the fore limbs slightly extended and the hind limbs relaxed. When drawn backward by the shoulders till the fore part of the body inclines posteriorly, the disturbed



Fig. 8.—Cat with lesion in the posterior vermis tested by being pulled backward. As the lobus pyramis is destroyed, the information as to its changed position, received from sight, the vestibular apparatus and the body cannot be coordinated, and as no attempt is made to maintain a proper equilibrium, the animal allows itself to recline backward, and when let go it falls on its back.

equilibrium is not appreciated, as the lesion in the lobus pyramis has destroyed the center in which the various afferent impulses concerned with the regulation of posterior balance are coordinated, so that there

is no counterbalancing contraction of the anterior muscles of the neck; and the posterior muscles of the neck acting unopposed pull the head farther backward, still further disturbing equilibrium, and as no attempt is made to reestablish the center of gravity forward by stepping backward, the body is allowed to lean backward and when suddenly let go the animal falls on its back (fig. 8).

In this experiment again, the symptoms are directly traceable to the lobe involved, for as the pyramis was destroyed the anterior muscles of the neck were thrown out of cooperation, and the primary cerebellar reflex resulted in the overcontraction of the unopposed posterior group. In the secondary response the limbs and trunk were brought into relation with this incorrect backward position of the head, further



Fig. 9.—The effect of a lesion in the left half of the lobus medius posterior of the middle lobe of the vermis. According to their reactions, each half of the lobe rotated the head toward the side that is stimulated. In this specimen, as the left half was destroyed, the right half, reacting without opposition, turned the head to the right.

increasing the disturbed balance, and as no effort could be made to regain its equilibrium, the animal naturally fell over backward.

*The Middle Lobe of the Vermis.*—In regard to the symptoms produced by the destruction of one half of the lobus medius posterior, it is of interest to note that this is probably the only instance in which a lesion of this lobe has produced any symptoms.

Ingvar's experiments<sup>6</sup> on the cat gave negative results, and my own early attempts were unsuccessful. But being convinced that

6. Ingvar, Sven: Zur Phylo- und Ontogenese des Kleinhirns nebst einem Versuch zu ein heitlicher Erklärung der cerebellaren Function und Lokalization, *Folia neuro-biol.* 11:205, 1918.

the reactions obtained on stimulating this lobe were correct, for they were found in both the cat and the monkey, the only possible explanation that would account for the absence of symptoms was that in making the lesion some of the folia belonging to the opposite side of the lobe were injured. And as the function of the two sides is to counterbalance each other, if both were cauterized there would naturally be no rotation of the head either way. In this last attempt, therefore, every precaution was taken to make certain that only the folia belonging to one side were destroyed. The results showed that this view was correct, and proved conclusively that the stimulation experiments did again accurately indicate the functions of the lobe (fig. 9).



Fig. 10.—Effect of a lesion in the dorsal lobule of the right lobus paramedianus. The reactions of this lobule to stimulation are confined to the region of the shoulder on the same side. Here there is ataxia in the right fore leg, it being raised too high, extended too far forward and brought too suddenly down. The tone in the limb is also increased, pushing the animal toward the opposite side.

In each of the preceding experiments a lobe was involved which was primarily concerned with equilibrium and the neck reflexes, the secondary response being shown in the altered tone of the limbs. But in the following instance the opposite condition will be found for the principal effect will be observed in the limb, the readjustment of equilibrium being secondary.

*The Lobus Paramedianus.*—In this experiment the lesion involved the dorsal lobule of the right lobe, the effect of which was to disturb the balanced activities of the muscles concerned in the forward and backward motions of the right shoulder. As a consequence, the muscles responsible for the forward movement, reacting without the proper opposition, raised the shoulder too high and brought it too far forward,

throwing the limb upward. Then, owing to the incoordination, for there was no paralysis, the effort to bring the leg down could not be properly synergized, and the movement was performed too suddenly. In this instance the primary reaction affected the limb, and as a result of the incoordination the tone in the fore leg was altered and equilibrium disturbed. The secondary response was the reestablishment of equilibrium through the cooperation of the whole cerebellum which reflexly adjusted the tone throughout the body (fig. 10).

#### SUMMARY AND CONCLUSIONS

The main facts brought out in this research are as follows:

1. The stimulation experiments, about which so many regrets have been expressed on account of the impossibility of having them confirmed by other investigators, are now proved beyond question to indicate clearly the function of the individual lobes.
2. The anterior vermis is definitely associated with the maintenance of forward balance, and if destroyed forward balance is lost.
3. The posterior vermis regulates backward balance, and if destroyed backward balance is lost.
4. The middle lobe of the vermis is concerned with the rotation movements of the head.
5. The loss of forward balance from a lesion in the anterior vermis, the loss of backward balance from a lesion in the posterior vermis and the rotation of the head to the opposite side when half of the middle lobe of the vermis was injured have shown in an indisputable manner that the vermis is divided into three lobes each of which has an entirely different function; the same three divisions also apply to the hemispheres and consequently to the cerebellum as a whole.
6. The function of the individual lobes, as indicated by the stimulation experiments, does not mean that the lobe is concerned only with that particular activity, but suggests that the lobe is responsible for whatever coordination is necessary to assure the proper performance of the act with which it is especially associated; e. g., the anterior lobe of the vermis gives reactions in the posterior muscles of the neck, the principal function of which is the maintenance of forward balance. When forward balance is disturbed this function is called into action and the first evidence of cerebellar activity is the posterior neck reflex, which provides for the necessary readjustment to take care of the threatened loss of equilibrium.
7. This indicates that cerebellar activity may be considered to be composed of two distinct reactions: (1) the primary reflex, the nature of which depends on the particular lobe involved, and (2) the secondary response, which integrates the synergic activity set in motion by the primary reflex.

8. The normal cerebellum always acts as a whole.

9. These investigations throw a new light on the question of equilibrium and the importance of the neck reflexes in regulating tone, and explain the mechanism of synergia.

10. The symptoms of cerebellar disturbance as indicated in this series of experiments are clearly explainable if the function of the lobes, as determined by their reactions to stimulation, are understood.

In this preliminary report on the effect of lesions of the individual lobes, a deliberate attempt has been made to confine attention to the fundamental facts that have been brought out in this particular research, viz., the disturbance of forward and backward balance, the rotation of the head, the dissociation in the shoulder movements and the question of the central control of the various impulses, which in the last analysis is responsible for the coordination on which every synergic activity depends.

Although the results of these investigations are in themselves of interest, of much more importance is the fact that a practical method of cerebellar exploration has been found which will make it possible to examine not only the function of each individual lobe, but the effect of lesions involving several lobes, until eventually every possible combination has been tried, and the influence of the different lobes on each other has been observed.

As in the stimulation experiments, the preliminary survey should be worked out on cats. Then with the experience thus gained the manner in which monkeys react to similar lesions should be examined.

If such a procedure could be systematically followed during the next few years, there is little doubt but that there would be a solution of most of those questions connected with cerebellar activity about which there is so much perplexity and the discussion of which with the present limited knowledge is so unprofitable.

#### ABSTRACT OF DISCUSSION

DR. FREDERICK TILNEY, New York: *Question.*—As practically every investigator has failed in his attempts to show that the cerebellar cortex is excitable, by electricity or otherwise, are the experimental results of cerebellar destruction competent to uphold the discrete regional excitability of the cerebellar cortex as shown by Dr. Mussen?

DR. AUBREY T. MUSSEN: *Answer.*—When it is recalled that Ferrier's systematic stimulation experiments on the rabbit, cat, dog and monkey gave results that are almost exactly similar to my own, when the difference in nomenclature is allowed for, and that his lesions of the anterior and posterior vermis also resulted in a loss of forward and backward balance, that Versilov, Prus, Probst, Lourie, Horsley and Clark, Bechterew, Rothman, Bárány and Hoshino, Dusser de Barenne and many others obtained reactions, though not so localized as mine, the evidence does not support the view that "practically every investigator has failed to show that the cerebellar cortex is excitable."

That the experimental results of cerebellar destruction do uphold the regional excitability of the cortex is proved by the effects of lesions in the anterior and posterior vermis. Stimulation of the anterior vermis causes contraction of the posterior muscles of the neck, pulling the head backward, and stimulation of the posterior vermis contracts the anterior muscles of the neck, pulling the head forward; the normal synergic activity of these two lobes regulates forward and backward balance. It follows, therefore, that if the anterior vermis is destroyed the posterior muscles of the neck will be thrown out of cooperation, so that the anterior muscles being freed from the antagonistic control of the posterior muscles will overact, disturbing the forward equilibrium, and the animal will fall over on its head. The same argument will apply to a lesion in the posterior vermis.

*Question.*—Are these two methods, stimulation and destruction, interchangeable and mutually confirmatory?

*Answer.*—Yes. The answer is summarized in the explanation of the first question.

*Question.*—Is it not true that large areas of the cerebral cortex yield no results on stimulation, but give rise to extensive functional disturbances when destroyed?

*Answer.*—It is possible that the parietal and occipital lobes which do not respond to stimulation would probably give rise to some functional disturbance if large areas were destroyed; but, on the other hand, I have kept monkeys for several months with both prefrontal lobes removed, and both Professor Alzheimer and Sir Frederick Mott, who examined them in Munich, could not distinguish them from normal monkeys.

*Question.*—Are not the facts brought out by stimulation one set of phenomena and those of destruction quite another? May this not explain why few if any investigators have obtained no results from stimulation, while almost all are agreed on a definite cerebellar localization as a result of destruction by injury or disease?

*Answer.*—The facts brought out by stimulation and those observed following destruction are quite in agreement up to the present time. That few experimenters have obtained definitely localized reactions is due to a number of clear reasons. The ordinary holder in which the head of the animal is gripped allowed of no movement whatever. Then the current was applied to the surface of the cortex and "spread" naturally resulted involving adjacent lobes with different activities. And as all the most usually examined areas of the cerebellum have been shown to be related to the activities of the muscles of the neck, and as these muscles are attached to the immovable head at one end and to a freely movable shoulder girdle at the other end, the natural result was that all stimulations produced such general reactions in the shoulders that no localization was possible. Again the importance of the finely balanced activities of the muscles of the neck in their relation to equilibrium has never been properly appreciated, so that to many observers the only response to stimulation was some indefinite movement of the shoulder. In my own experiments the conditions were entirely different. With the stereotaxic instrument free movement of the head is provided for, and by applying the current to the Purkinje cells, instead of to the cortex, a reaction from the cells of that particular folium was obtained, and consequently a localized response was observed.

In referring to the definite localization due to injury or disease, I think that the questioner must have in mind extracerebellar conditions.

*Question.*—It seems to me that your recent experiments have abundantly proved a localization of function in the cerebellum and also the general synergic character of this function. It is difficult for me to believe that an organ which you and many others have shown to operate in the interest of cooperation and posture would function in highly discrete areas.

*Answer.*—To me the difficulty would be to understand how an organ on which the synergic activity of all motor function depends, including the maintenance of equilibrium, could operate at all unless it was able to function in discrete areas.

The only clear explanation of cerebellar function lies in the fact that each individual lobe represents some definite activity which is regulated by the controlling influence of an antagonistic lobe. It is the normal functioning of these complementary lobes that produces synergic reactions. This is illustrated in a simple form when a normal cat jumps from a table; there is first the anterior neck reflex which by regulating the tone in fore and hind limbs determines the power necessary for the act, then as soon as the jump has been made the posterior neck reflex begins to operate under the changing impressions from sight and the vestibular apparatus so that equilibrium during the flight may be correctly maintained, and finally by means of its greater activity it throws the head farther backward, thus increasing the tone in the fore limbs in preparation for the shock of landing.

*Question.*—My feeling is that the cerebellum functions in extensive cooperations with preferential emphasis on the part or parts which play the leading rôles in each succeeding posture.

*Answer.*—The truth of this assertion is clearly demonstrated in the action of a normal cat jumping from a height. Each posture of the body and the necessary alteration in tone are preceded by the associated and regulating neck reflex.

*Dr. Tilney.*—I have obtained so much help and inspiration from Dr. Mussen's work that I am anxious for him to clear up all points of doubt in my mind. I may therefore be forgiven if I ask for more light on the cerebellar localization determinable by electric stimulation, and also if I doubt that there is a discrete localization in the cerebellum comparable to the exquisite localization in the motor cortex to electricity. I am sure that we are all deeply grateful to Dr. Mussen for his sturdy efforts in leading us to a better understanding of the cerebellum.

DR. THEODORE H. WEISENBURG, Philadelphia: The whole problem of cerebellar localization depends entirely on how one views cerebellar activity. There are two schools of thought; those, for example, who believe that the cerebellum does not act independently, and those who believe that the cerebellum acts from the standpoint of localization. My own conception is something like this: The business of the cerebellum is to coordinate the activity which is initiated in the cerebral cortex, in the striatum or in the midbrain. Every portion of the motor apparatus, and I am including the cerebellum as part of the motor apparatus, functions all the time. If there is a lesion in one part of the cerebellum, that particular part of the cerebellum can no longer function, and whatever the patient is able to do is because of the unimpaired activity of the remaining part of the motor system in which the cerebellum is a distinct part. With this point of view it is possible to coordinate the views of Dr. Tilney and Dr. Riley that the cerebellum always acts as a whole. It seems to me, therefore, with this point of view, that one can readily coordinate what Dr. Mussen has found from stimulation experiments with what he has obtained as a result of deficit experiments. In other words, one must never believe that the cerebellum can act alone, but that it always acts with every other part of the whole great motor system.

DR. AUBREY T. MUSSEN: Dr. Weisenburg has expressed so clearly the same idea to which the results of my experiments have led me that I should like to emphasize his views. He says, in effect, "My own conception is that the function of the cerebellum is to coordinate the activity which is initiated in the cerebral cortex, the striatum or the midbrain; and that every portion of the motor apparatus including the cerebellum functions all the time. And when there is a lesion in one part of the cerebellum, as that particular part can no longer react, whatever the patient is able to do is because of the unopposed activity of the remaining parts."

The truth of these remarks is fully illustrated by the experiments that have just been reported. For the manner in which an intact cat jumps from a table demonstrates most perfectly the coordinating mechanism of forward and backward balance, when the cerebellum acts as a whole. But when there is a lesion in the anterior vermis and the cat in jumping from a height falls forward, then the symptom of this loss of forward balance is due to the unopposed and consequent overactivity of the remaining parts. In this case it is the posterior vermis, for it has been shown that this region of the cerebellum controls the anterior muscles of the neck, which being unopposed react too strongly, producing an excessive anterior neck reflex, with its diminished tone in the fore limbs and increased tone in the hind limbs. *Mutatis mutandis*, the same explanation will apply when the lesion is in the posterior vermis, the middle vermis or the lobus paramedianus.

In these researches there are for the first time several cases in which lesions have been definitely localized to individual lobes, and the subsequent effects carefully observed. In each case the symptoms that occurred were the result of the overaction of the unopposed antagonistic or complementary lobe. This suggests that the disturbance caused by intracerebellar disease should be considered as an indication of the overactivity of the normal lobes and not as the symptom of the part affected. Not until this complementary relationship between the cerebellar lobes is clearly understood will it be possible to explain the pathology of intracerebellar disease.

## DISSEMINATED ENCEPHALOMYELITIS

ITS RELATION TO OTHER INFECTIONS OF THE NERVOUS SYSTEM \*

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Either clinicians have become more observant of various types of infections of the central nervous system in the last decade, or there has been a decided increase in the number of such infections. Since the pandemic of encephalitis (von Economo's disease), postvaccinal encephalitis has become a definite entity; encephalitis following measles, variola and varicella has been called to attention, and disseminated encephalomyelitis has definitely increased (Redlich <sup>1</sup>).

In addition to controlling the clinical diagnosis, the neuropathologist attempts to discover the pathogenesis of the disease that he is studying. His rôle in establishing the infectious nature of a syndrome should be invaluable in the search for the etiologic agent. That he cannot fulfil this function is apparent to the critical-minded, since there exists no degree of unanimity of opinion as to whether any of these forms results from toxic, degenerative or infective virus causes. Yet these encephalitides have been compared with one another and their similarities and differences stressed in an attempt at classification, without toxic, bacterial or virus etiology having been proved for any type. As Spielmeyer <sup>2</sup> so lucidly stated, progress can be made in the study of new diseases only on the basis of what has already been learned from the pathology of etiologically proved infections. Even then it is difficult to make a pathologic differentiation, for several infectious diseases may produce an almost identical reaction in the host, as, for example, Heine-Medin's disease and rabies.

In view of the frequent pathologic comparisons of one form of supposed virus encephalitis with another and their classification into

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\* Read at the Fifty-Sixth Annual Meeting of the American Neurological Association, Atlantic City, N. J., June 9, 1930; see discussion following paper by Ferraro and Scheffer, p. 778.

1. Redlich, E.: Ueber ein gehäuftes Auftreten von Krankheitsfällen mit den Erscheinungen der Encephalomyelitis disseminata, *Monatschr. f. Psychiat. u. Neurol.* **64**:153, 1927.

2. Spielmeyer, W.: Infektion und Nervensystem, *Ztschr. f. d. ges. Neurol. u. Psychiat.* **123**:11, 1930.

probable etiologic types, we shall report several recent examples of encephalomyelitis, compare them with examples of other forms of encephalitis that we have personally studied, propose a broad pathologic classification, and outline the etiologic conclusions that are justifiable in the light of present knowledge.

#### REPORT OF CASES

*CASE 1.*—*Slight upper respiratory tract infection; five days later, bulbar and cord symptoms with low grade fever; death from medullary involvement in nine days; multiple perivascular softenings throughout the neuraxis.*

*History.*—A woman, aged 23, who entered the Billings Hospital on Feb. 16, 1929, had been in good health except for appendicitis and complicating peritonitis ten years previously. Three weeks before admission, she had been married. A week later, she contracted a heavy "cold" characterized by hoarseness and a slight nonproductive cough, but without fever. On February 12, she fell asleep with her feet hanging over the rung of a chair. On awakening, the feet felt "sleepy," but there was no other complaint until that evening, when she felt generally ill and could not urinate or defecate. The next morning, the feet felt cold and the temperature had risen to 99.5 F. On February 14, the patient was drowsy and could not swallow liquids or solids without choking. Diplopia was noted, and violent oscillatory ocular movements were observed on upward gaze. The urinary retention continued, and the temperature remained at about 100 F.

*Examination.*—The pupils, although equal and regular, reacted poorly to light and in accommodation. There was a fine, rapid synchronous oscillation of both eyes when they were first fixed on an object or suddenly shifted. After fixation was accomplished these movements would cease. There was weakness of the left external rectus muscle; the left side of the palate drooped, and both pharyngeal and palatal reflexes were absent. The speech was nasal, and liquids and solids could not be swallowed without choking. A thick mucoid material in the upper part of the respiratory tract could not be raised by the patient. The upper deep reflexes were normal, as were also muscle tone, power, coordination and sensation, but there was a coarse action tremor of both hands. There was foot drop on the right side, and the toes could not be moved. Both legs, especially the right, were weak in all movements. The right knee jerk was diminished, and the ankle jerk absent. Tactile and vibration sensations were especially reduced on the right leg and absent on the right foot, although all modalities of sensation were decreased.

*Course.*—On February 18, there was evidence of bronchopneumonia. On February 19, there were: marked weakness of the right side of the face, definite bilateral ptosis of the upper lid, a temperature of 103 F. and other conditions as before. That evening the patient became cyanotic and died.

*Laboratory Studies.*—The urine contained a large quantity of acetone. The red blood cell count was 4,050,000 per cubic millimeter; the white cell count was 12,000, of which 80 per cent were polymorphonuclear leukocytes. Lumbar puncture yielded clear, colorless fluid under no increased pressure. The Ross Jones test gave negative results; only 5 cells per cubic millimeter were counted, and the Lange gold curve was flat. A determination of spinal fluid sugar gave 72 mg. per hundred cubic centimeters, and the Wassermann reaction was negative. Cultures from the throat were negative.

*Anatomic Diagnosis.*—The diagnosis was subacute proliferative peribronchitis and pulmonitis (postinfluenzal?) and bilateral hypostatic bronchopneumonia.

*Macroscopic Examination.*—The central nervous system showed many grayish-yellow areas scattered irregularly on the cut surfaces of the spinal cord and medulla. The entire surface of the sacral portion of the cord was discolored in this manner. Both the pial and the cut surfaces of the brain and spinal cord were hyperemic.

*Microscopic Studies.*—The leptomeninges were diffusely infiltrated with a moderate number of lymphocytes, with a slight increase in the endothelial cells. The lymphocytes were especially numerous where the underlying tissue contained a characteristic lesion. The pial vessels were all engorged with blood. Many fat-



Fig. 1 (case 1).—Sacral cord, showing the softenings at the pial margins. Note the meningeal infiltration. Scharlach R;  $\times 50$ .

filled gitter cells were found in the pia-arachnoid, mixed with the lymphocytes. With scharlach R stains there was an unusual condition in the myelin sheaths of the sacral roots. They showed evidences of early fatty change without fragmentation or loss of shape.

The characteristic lesions to be described were distributed throughout the entire cord and brain, but were most numerous in the medulla and the sacral part of the cord (fig. 1). The subcortical white matter was studded with many typical perivascular lesions of only minute size. The tegmentum of the medulla was severely damaged, and in one area the posterior longitudinal bundle seemed practically destroyed. In the spinal cord the perivascular lesions were situated in both the gray and the white matter, but mostly in the latter. Of the white substance,

the peripheral areas, including the structures adjacent to the medial fissures, were most affected. In the cervical region the base of the posterior columns was destroyed.

Everywhere the detailed structure of the lesions was identical, varying only in degree. The lesions were all in direct relation to a blood vessel of the venous type (fig. 2). In longitudinal sections the lesions were seen to extend as far as the vessel could be followed and to disappear with it. Frequently, lesions coalesced with adjacent lesions to form large softenings (fig. 3). The central venules of the foci were infiltrated with a moderate sized cuff of lymphocytes mixed with a few plasma cells, but many fat-filled gitter cells. The surrounding

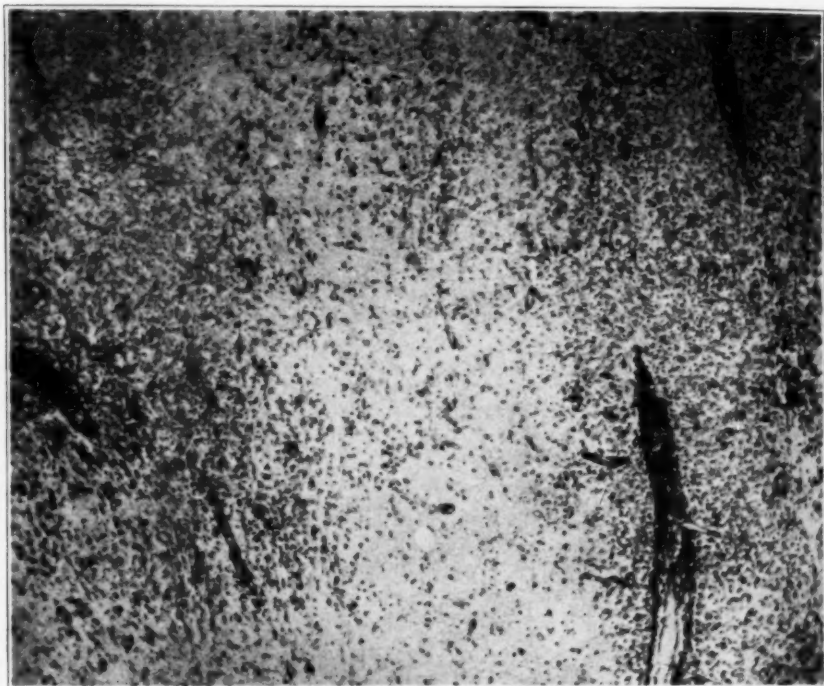


Fig. 2 (case 1).—Multiple perivascular softenings. The areas filled with microglia and the gitter cells tend to coalesce. The central venules are infiltrated with phagocytes and lymphocytes. Scharlach R;  $\times 60$ .

tissue was either completely or incompletely softened. The myelin sheaths were entirely disintegrated, so that for the most part no myelin globules remained. Only occasionally the borders of a lesion revealed a few fenestrated myelin sheaths or faintly stainable myelin balls. The axons apparently were completely destroyed in the older areas, whereas in others they were only markedly swollen and greatly fragmented. In the younger lesions some apparently healthy axons were seen.

The softened tissue was filled with microglia in all stages of development into rounded-out, fat-filled, gitter cells. The processes of the young microglia were clearly outlined by their fat content. Much free fat in the form of varying sized globules were found free in the tissue. The older lesions contained many young

astrocytes with very small and fine processes. No connective tissue was found outside of the walls of the vessels.

Although the gray matter was also involved, the ganglion cells were spared. Entirely healthy cells were found in the midst of serious fiber destruction (fig. 4). Small patches were found in the basal nuclei and subcortical white substance. The substantia nigra was normal. The cortical cells showed only moderate swelling and chromatolysis.

*Comment.*—In this patient, without antecedent illness, extending medullary and cord symptoms developed rapidly following an infection

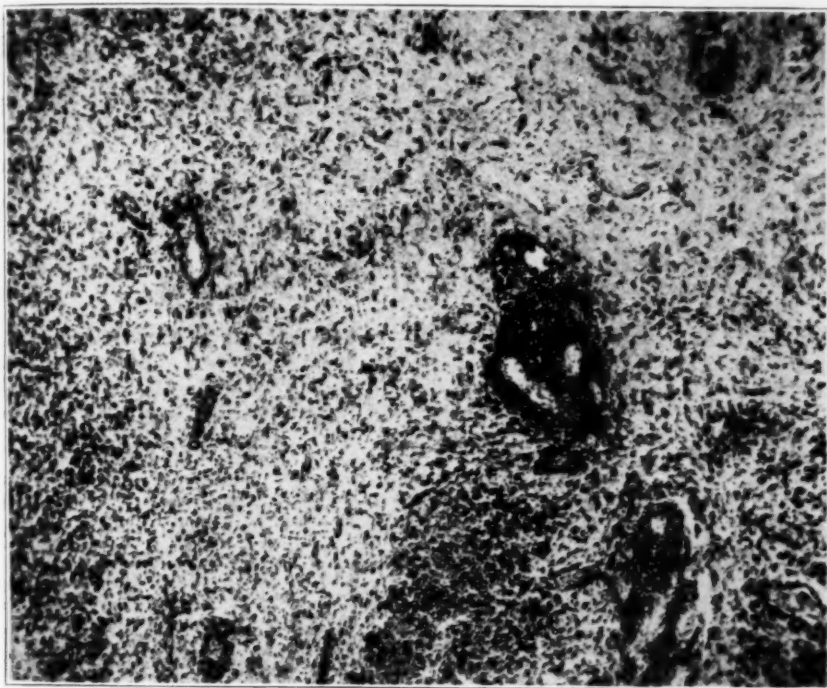


Fig. 3 (case 1).—Higher power photograph of the perivascular softening. The proliferated microglia outlined by their fat content may be seen. Scharlach R;  $\times 60$ .

of the upper respiratory tract. It was made certain that no exanthematous disease or vaccination had occurred. There was little evidence of progression of the cord or bulbar symptoms after they were manifested, the lethal end being determined largely by bronchopneumonia due to aspiration. The location, therefore, of the initial lesions probably determined the fatal outcome. Little difficulty in the diagnosis was encountered as all signs pointed to disseminated inflammatory lesions of the central nervous system. The absence of meningeal symp-

toms and spinal fluid pleocytosis with such an extensive infection and the low grade fever were against the diagnosis of Heine-Medin's disease.

Yet, anatomically, the expected usual appearance of a disseminated encephalomyelitis was not encountered. Rather, the entire picture was identical with that which has been described in encephalomyelitis following the use of cowpox vaccine and rabies vaccine, and in encephalitis fol-

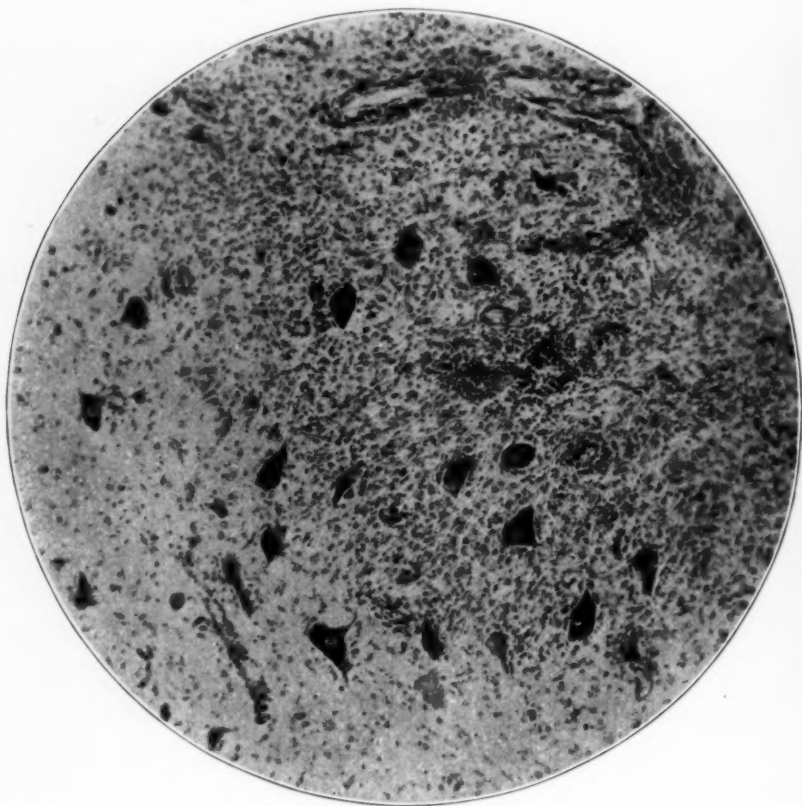


Fig. 4 (case 1).—An incomplete softening in the medulla. The ganglion cells adjacent to and within the lesion are normal. Cresyl violet stain;  $\times 90$ .

lowing measles and variola. The perivascular, inflammatory, complete and incomplete softenings with moderate lymphocytic reaction are typical of these forms of infections. A predilection for the peripheral areas of the cord, as Wohlwill described in his case of measles, was also encountered. Are all these cases, then, examples of identical virus infections only precipitated by exanthematous disease, vaccinations and nonspecific infections, such as upper respiratory infections? As this article was

being completed, Greenfield's<sup>3</sup> study of the only two similar cases in the literature was published. His cases occurred after influenza, in February and March, 1929, about the same time as our case; our studies were made independently, and the identity of the changes in the brain with those of postvaccinal encephalitis was recognized by both. Greenfield expressed the belief that his cases demonstrate that the pathologic syndrome represents a disease per se, stimulated by vaccination, exanthematous diseases and other infections.

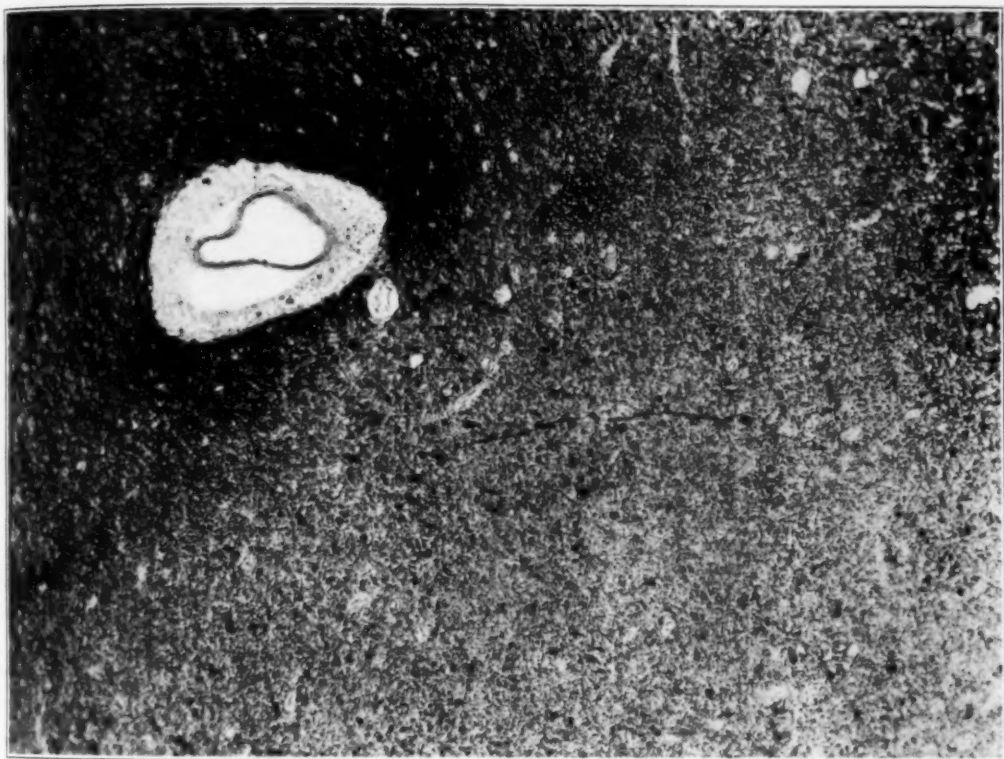


Fig. 5 (case 2).—A patch of almost complete demyelination in the deep white matter. Note the vaguely defined borders of the lesion and the absence of mesodermal infiltrations. Myelin sheath stain;  $\times 100$ .

*CASE 2.*—In a child, leg paresis and hemiplegia developed gradually; the opposite leg became involved; stupor; terminal fever led to death in twenty-three days after the onset; disseminated encephalitis.

*History.*—A girl, aged 10, was brought to the office of Dr. B. Gasul on July 29, 1929, with the complaint of difficulty in walking, especially with the left leg, for one week. Her previous personal and family histories were unimportant.

3. Greenfield, J. G.: Acute Disseminated Encephalo-Myelitis as a Sequel to Influenza, *J. Path. & Bact.* **33**:453, 1930.

*Examination.*—The child was apparently healthy, with a normal pulse rate and temperature. Neurologic examination disclosed paresis of the left leg, so that it dragged on walking. The left knee jerk was exaggerated; the left abdominal reflexes were absent, and there was a positive Babinski sign on the left. All other observations, including the usual laboratory tests of the blood and urine, were negative.

*Course.*—On August 10, the patient was seen again at home; she had become gradually weaker and finally unable to walk. She was stuporous. On removal to

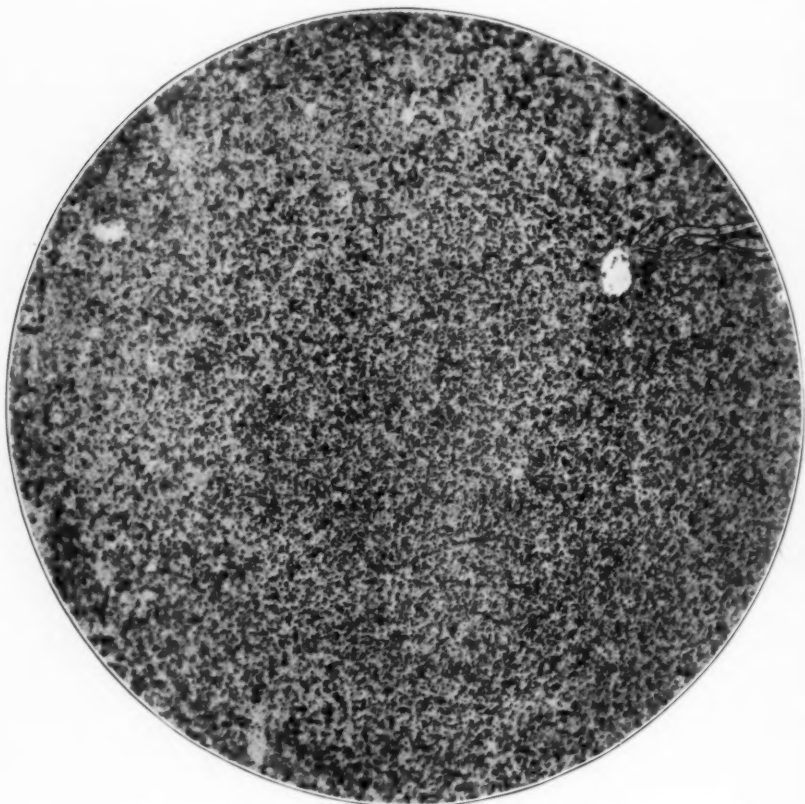


Fig. 6 (case 2).—A focus of demyelination, showing the intracellular and extracellular fat. There is no mesodermal vascular reaction. Scharlach R;  $\times 75$ .

the hospital it was discovered that the left arm and leg were paralyzed and spastic while the right leg was paretic. All of the deep reflexes were exaggerated, and a bilateral Babinski sign was then obtained.

The temperature was 99.8 F.; the urine was normal; the white blood cell count was 14,250 per cubic millimeter. The spinal fluid was normal, save for a sugar content of 90 mg. per hundred cubic centimeters. The child became comatose, the temperature rising to 103 F., and death occurred on August 13, twenty-three days after the onset.

*Laboratory Observations.*—Macroscopically, the brain was normal. Microscopically, the leptomeninges revealed only slight thickening but no infiltration or exudation. With myelin sheath stains, small areas of complete and partial demyelination were found scattered in the subcortical white matter (fig. 5). Some were rather sharply demarcated from the adjacent normal tissue, while others were poorly defined, giving a moth-eaten appearance to the section. These lesions were also present in the subcortex just below lamina VI and involved the U fibers. No patches in the cortex or basal nuclei were found, and the brain stem was also free from lesions.

Closer study showed the lesions to be areas of partial demyelination for the most part. The myelin sheaths were severely altered, with fenestration and the

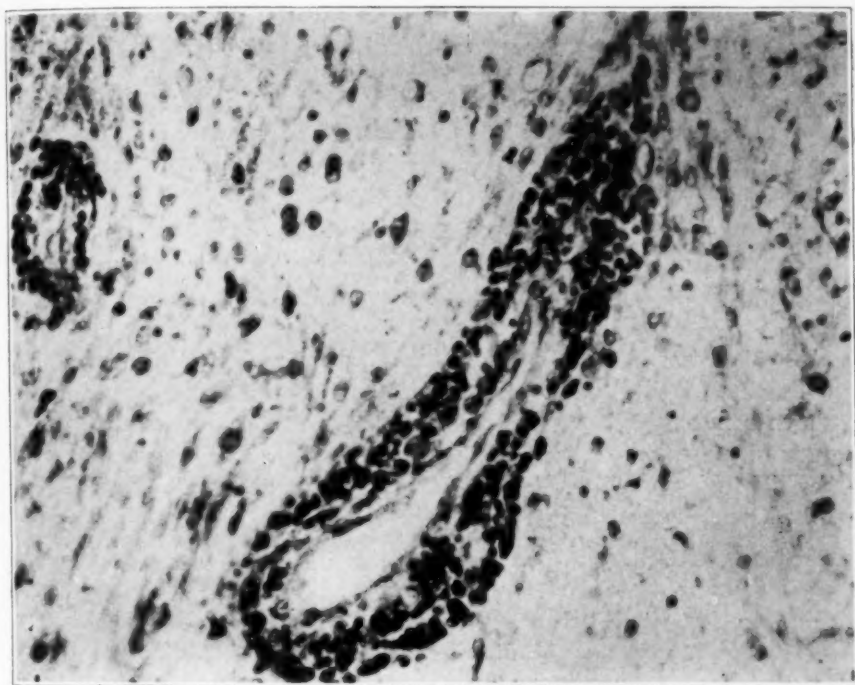


Fig. 7 (case 2).—A venule from the deep white matter, showing the perivascular infiltration of plasma cells and lymphocytes. There is no adjacent softening, but note the increase in microglia and astrocytes in the tissue. Cresyl violet stain;  $\times 310$ .

formation of myelin balls, but many still preserved their structure and took hematoxylin stains. The areas were not perivascular in distribution, and in the damaged areas there were only capillaries and precapillaries which contained no mesodermal infiltrations. The lesions were filled with fat-containing gitter cells mingled with the remains of myelin (fig. 6). The axons were relatively preserved; but swollen, tortuous and frequently fragmented. Free fat was present in the tissue, and the adjacent vessel walls were clustered with gitter cells. In the neighborhood of the foci an increase in astrocytes was noted, but no large "ameboid" glia or other regressive glia forms were noted.

Diffusely throughout the brain and brain stem, including the gray cortex, the larger blood vessels, venules and arterioles were infiltrated with mesodermal elements (fig. 7). For the most part these were plasma cells, but many lymphocytes were also noted. These infiltrated vessels had no relationship with the softenings, but in their vicinity an edema of the glia "feltwork" could be noted with an increase in astrocytes and microglia.

*Comment.*—The multiple areas of demyelination and incomplete softenings resembled the early lesions of multiple sclerosis. No dependence on the blood supply was noted, but the lesions showed no stimulation of astrocytes in an attempted gliosis nor any regressive glial forms so characteristic of Schilder's disease, nor were the size and locations of the lesions compatible with such a diagnosis. The rapid clinical course of a diffuse damage to the brain in a child of course suggested this possibility. The widespread inflammatory reaction not associated with the lesions, hence not a secondary inflammation, made the probable pathologic diagnosis one of disseminated encephalitis.

The extraordinary dissociation of the inflammatory reactions and the patches of demyelination are the high points of interest in this case. The diffuseness of the infiltrations, the character of the cells and their presence distant from the lesions surely suggest infection. The foci alone, however, if one compares the lesions with multiple sclerosis and Schilder's disease, would cause many to conclude them to be of toxic degenerative origin. Are there two factors at the basis of the pathologic changes, or is the whole process infectious? That question, in the light of present conflicting views as to the nature of the changes described, is unanswerable.

*CASE 3.—Severe acute medullary symptoms with low grade fever, several remissions over a period of five months, progression with cord symptoms and death; subacute disseminated encephalomyelitis.*

*History.*—A woman, aged 21, had been well until Oct. 20, 1928, when she was suddenly taken ill with vertigo, vomiting, diplopia and tinnitus. In a few days a fever of from 99 to 100.2 F. developed. On October 27, an otologist found lateral nystagmus, but normal hearing. On November 10, a neurologic examination revealed only the lateral nystagmus and a voluntary immobility, as all movements induced nausea and vomiting. Ten days later, a lower neuron type of facial paralysis developed on the right side. On November 23, taste was absent in the anterior part of the right side of the tongue, the right ear was deaf, and shortly thereafter a right external rectus paralysis and difficulty in swallowing developed. In December, the facial palsy had subsided, but ataxia of the right arm and leg had developed.

At the end of December, taste and facial movements were normal, nystagmus and vertigo were decreased and hearing had returned. There was less right-sided ataxia, but the left arm and leg were weak. During January, walking with support was possible and the left-sided paresis had improved. In February, short, frequent (thirty a day) clonic spasms of the right side appeared, with

weakness of the right arm, nystagmus again, blurring of the nasal sides of the disks, bilateral Babinski sign and absent abdominal and exaggerated tendon reflexes. On February 25, the right arm was paralyzed, the right leg was paretic and sensibility to pain and temperature was lost on the left side.

On March 10, the patient became much worse, with nausea, dizziness, diplopia and vomiting. There was bilateral knee and ankle clonus; a horizontal nystagmus was present, and low grade bilateral optic neuritis gradually developed. Examination of the spinal fluid then gave entirely normal results.

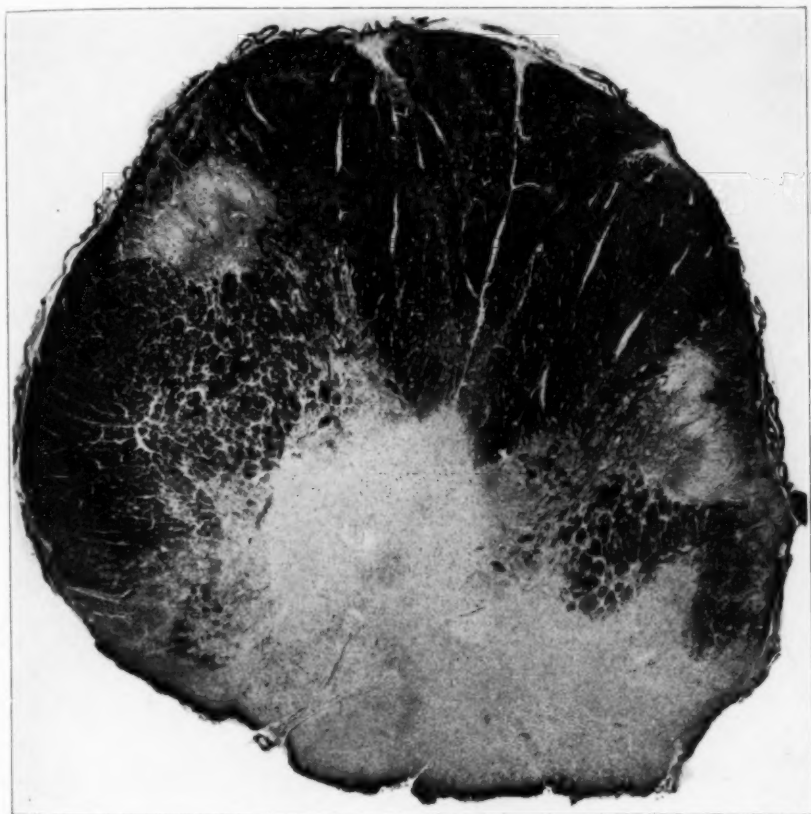


Fig. 8 (case 3).—The medulla, showing the large coalescing lesions. Myelin sheath stain;  $\times 8$ .

During the next few days, cervical rigidity was found, speech became more nasal and the tongue deviated to the right, although swallowing improved for a time. On March 18, difficulty in swallowing became worse, and respiratory distress and cyanosis set in; the left side was almost entirely paralyzed. Death occurred on March 20, 1929, five months after the onset.

*Macroscopic Examination.*—The brain and spinal cord showed no abnormalities.

*Microscopic Examination.*—The location of the characteristic lesions was found to be in the regions of the pons, medulla and cerebellar peduncles in the

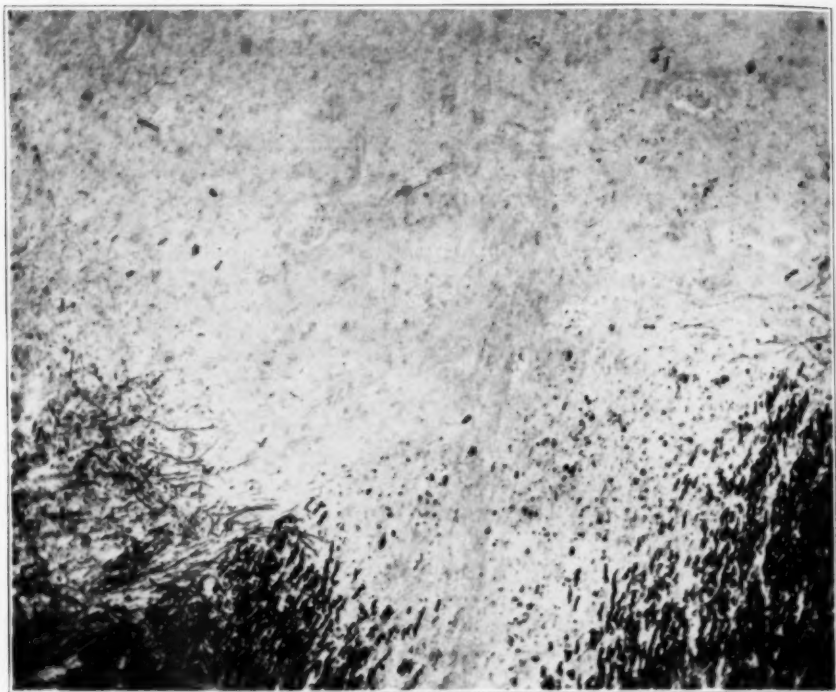


Fig. 9 (case 3).—A demyelinated patch, showing the partial myelin destruction at the periphery, evidence of extension of the lesion. Myelin sheath stain;  $\times 60$ .

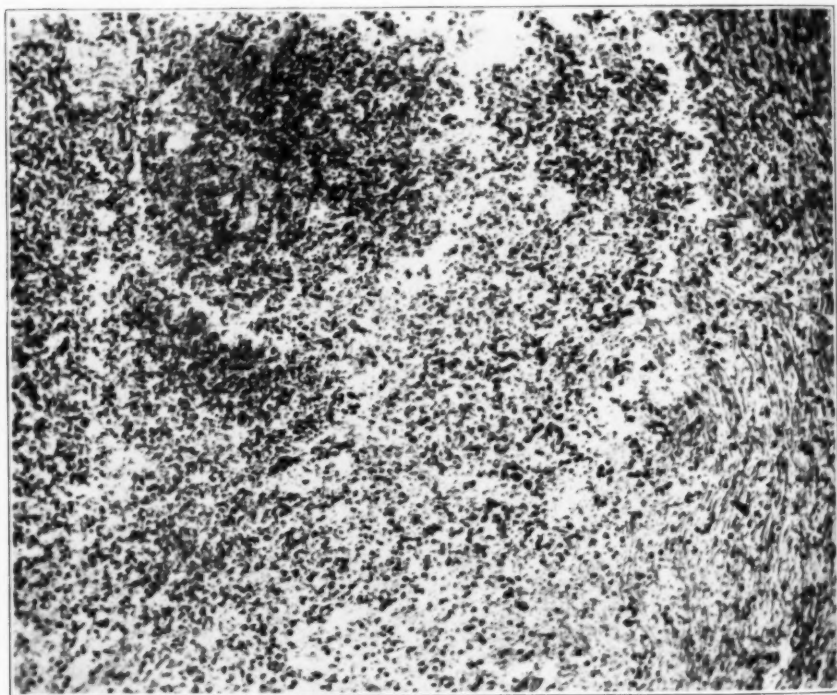


Fig. 10 (case 3).—A complete softening. Note the sharp boundary of the focus although the adjacent nerve fibers are swollen. Scharlach R;  $\times 60$ .

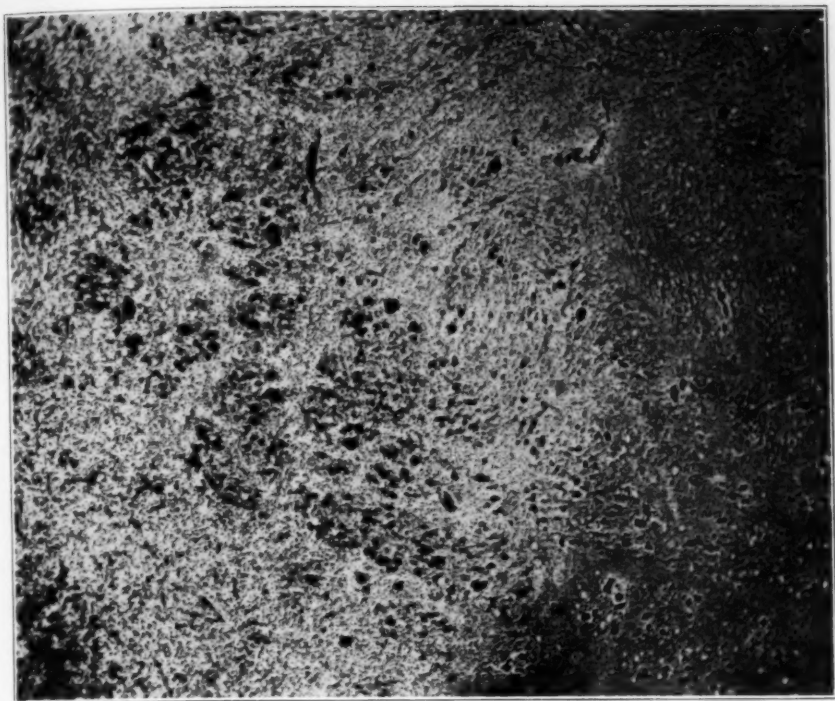


Fig. 11 (case 3).—Marked axonal fragmentation and destruction in a patch. There are fine and coarse argentophilic fragments. Bielschowsky;  $\times 60$ .

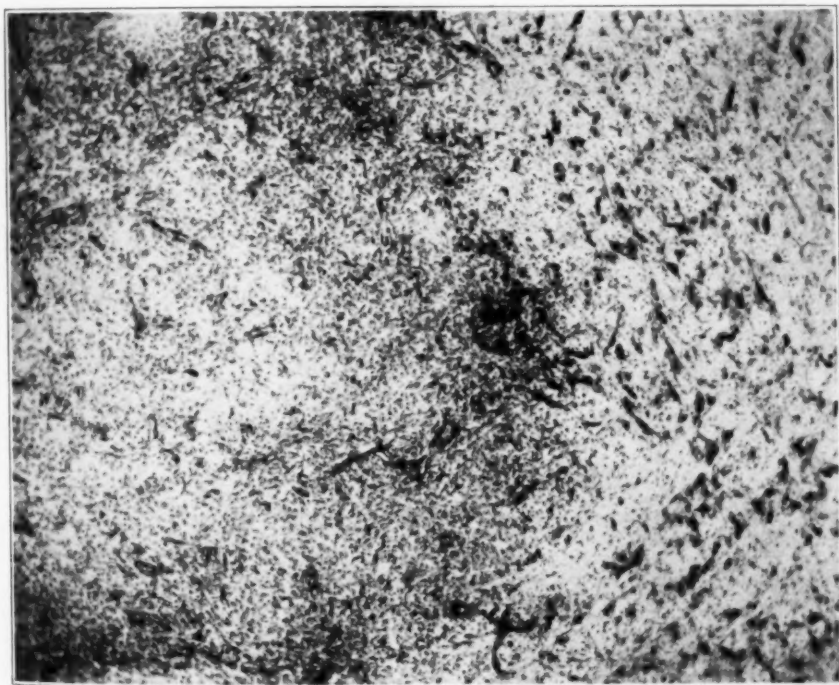


Fig. 12 (case 3).—A sharply defined old lesion. Many fibroblasts are mingled with the gitter cells. There is no gliosis. Cresyl violet;  $\times 60$ .

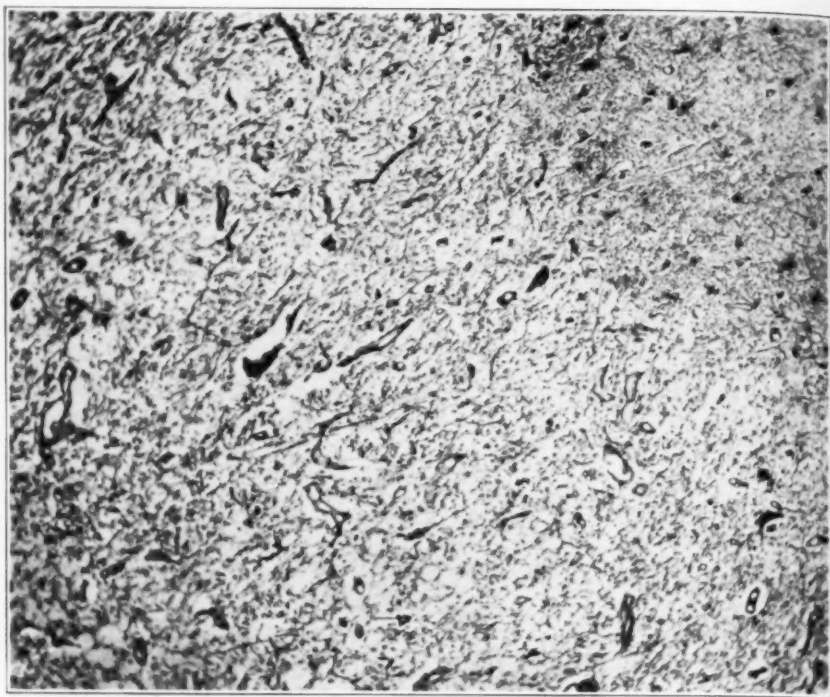


Fig. 13 (case 3).—A patch from the medulla, showing the proliferated blood vessels with markedly increased reticulin. Many gutter cells are in the background. Perdrau;  $\times 60$ .

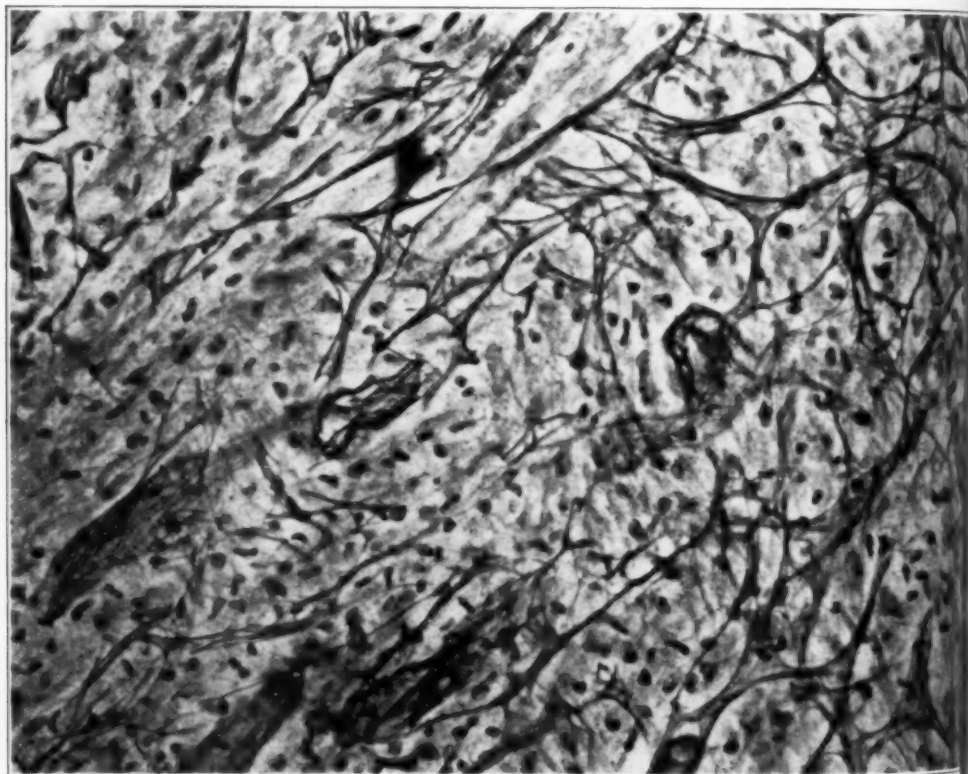


Fig. 14.—Higher power photograph of figure 6, showing the extension of connective tissue and young fibroblasts into the tissue and the absence of a glial sclerosis. Perdrau;  $\times 300$ .

greatest number and extent, but the upper cervical cord also showed patches. Otherwise the brain and spinal cord showed no large lesions. The cortical cells revealed a moderate degree of swelling, not incompatible with preagonal changes. The substantia nigra was normal.

The lesions consisted of large patches of complete demyelination (fig. 8). In the centers of such areas only a few myelin shadows could be seen. At the peripheries, however, although the lesions were sharply defined, the myelin sheaths revealed the various phases of fresh degeneration (fig. 9). The myelin was replaced by simple fats and in scharlach R stains large quantities of fat were found free in the tissues and intracellularly in microglia which were in all stages of conversion into gitter cells (fig. 10). The gitter cells were also clustered in the perivascular spaces of the adjacent blood vessels.

The lesions themselves may be spoken of as complete and sometimes incomplete softenings. The nerve fibers were as completely destroyed as the myelin sheaths even in those areas that were apparently early lesions (fig. 11). Lymphocytes were abundant in the perivascular spaces and in the leptomeninges adjacent to the lesions. In the larger, completely softened areas a large amount of homogeneous colloid material was present free in the tissue.

The areas near the lesions revealed an infiltration of myelophages between healthy fibers, which had apparently migrated from the lesion. No early myelin destruction could be seen here. The early lesions showed also an increase in astrocytes mingled with the gitter cells. These had undergone early regressive changes and were "gemästete" in type. The patches had no correlation with a definite arterial supply, and did not seem to be perivascular in distribution. The blood vessels were markedly thickened with reticulin which was meshlike and enclosed pockets of gitter cells. The older lesions were filled with young fibroblasts and a small amount of reticulin (fig. 12, 13 and 14).

*Comment.*—The clinical observations indicated clearly that the sites of the lesions were in the brain stem. The nature of the pathologic process was surmised from the suddenness of the onset, the febrile reaction and the relatively rapid course. Yet remissions were present during the five months of the disease, during which severe bulbar symptoms almost entirely disappeared. Anatomically, large, patchy, complete and incomplete softenings were found, sharply demarcated with moderate inflammatory reaction and connective tissue "scar formation." Certainly very little was reminiscent of what is known as multiple sclerosis with its initial myelin damage and secondary gliosis, yet just as few signs of primary inflammation could be found here as in multiple sclerosis. Of course, the material was studied when the lesions were old, and we cannot conclude that the myelin was not first and intermittently attacked, thus explaining the remissions. The disease advanced by extension of the old lesions at their peripheries, and no multiplicity of fresh lesions could be found.

*CASE 4.*—A previous acute infectious episode with medullary symptoms; recovery with severe residua; relapse with febrile reaction.

*History.*—A man, aged 42, entered the Billings Hospital on Feb. 13, 1930, stating that he had been perfectly well until the summer, 1927. In August, 1927,

bronchitis with vomiting, excessive salivation and intention tremor of the right arm developed. He recovered from the febrile attack in two weeks; over a period of two months a staggering gait, inability to control the right arm sufficiently to write, diplopia and difficulty in swallowing and speaking gradually developed. Subjective numbness of the right arm and leg also appeared gradually. In the intervening two years, no remissions occurred, but the symptoms described had all moderately increased in severity.

*Examination.*—The patient was well developed and not acutely ill; he walked with a broad base and considerable uncertainty, and swayed in all directions. The Romberg test gave positive results. The pupils were equal and reacted normally. There was no spontaneous nystagmus, but on left lateral gaze there was a slow coarse clockwise rotatory nystagmus. On looking to the right, the nystagmus was much quicker and finer, while on looking upward the movements were as those on looking to the left. There was a left external rectus weakness, with diplopia so bothersome that a black eye patch was worn. Speech was indistinct and nasal, the pharynx insensitive and the left vocal cord was completely paralyzed. There was a large colloid goiter, although the basal metabolic rate was plus 5 per cent. Pronounced weakness of the left side of the face of the lower neuron type was noted, and there was a right hemiparesis with absent right abdominal reflexes, positive Babinski sign and ankle clonus. The sense of position was impaired in the right upper extremity.

*Course.*—On the second day of hospitalization, a fever of 102 F. developed, without demonstrable cause. During this period all neurologic signs became worse. The external rectus paresis increased in degree, speech became less clear, salivation appeared and staggering was more pronounced. Examination of the spinal fluid during this period showed no abnormalities. The fever and general malaise gradually receded, and the patient was discharged somewhat worse as regards all complaints, but without evidences of new lesions.

*Comment.*—It seems probable that in 1927 the patient had an acute disseminated encephalomyelitis with severe damage of the medulla, especially on the left side. In two years he showed slight increase in disability, and while in the hospital a second febrile attack occurred with progression of preexisting lesions. This could mean only an extension of the inflammatory softenings, perhaps at the peripheries, as pathologic studies in case 3 would indicate, rather than the formation of new lesions. One can hardly speak of a single attack that crippled or killed in either case 3 or in case 4, as in one case remissions took place, and in both progressions were undoubted.

#### COMMENT

We shall discuss what justifiable conclusions may be drawn from pathologic studies such as those we have made. The correlation of the site of a lesion in relation to the clinical symptoms it produces, the so-called "pathophysiologic" conclusions, are not of prime significance here. We are concerned with the ability or possible inability to differentiate degenerative from infectious pathologic changes. Can one indicate to the bacteriologist or worker among the filtrable viruses on

which diseases he should concentrate attention because of their undoubted infectious nature?

The large group of diffuse encephalitides cannot, of course, be discussed without giving a prominent place to Schilder's group of encephalitis periaxialis diffusa. Already, seventy cases in which necropsy was made have been studied and have lately been reviewed by Gasul.<sup>4</sup> In general, the whole pathologic syndrome is characterized by wide-spread early demyelination, later appearing but profound axonal destruction and proliferation of astrocytes which show regressive changes to form the so-called "gemästete Glia." The attempt at gliosis simultaneously with "Abbau" of lipoids by microglia is short lived. The scarring of the old lesions is done by connective tissue and the glia that is not yet destroyed. The individual cases seem to vary in the mesodermal infiltrations; some show a large amount of lymphocytic and plasma cell perivascular infiltration, while others may show practically none. Globus and Strauss<sup>5</sup> called the disease a degenerative encephalopathy, as they considered the inflammatory signs secondary to the tissue destruction. Schaltenbrand,<sup>6</sup> however, expressed the belief that there is a primary inflammation, and that the process is infectious. Bouman<sup>7</sup> attempted to straddle the issue by classifying the cases with many lymphocytes as infectious, the others as degenerative. Such a criterion of infection has pervaded the literature and has been used in other diseases, such as multiple sclerosis. Its lack of significance in such a uniform clinical group and pathologically related series of cases as Schilder's disease makes its significance doubtful. One may as well classify cerebral softenings by the presence or absence of lymphocytes within the adjacent vessel walls. Such secondary inflammation has naught to do with the primary thrombotic process.

With the exception of the perivascular infiltrations, which may depend on the quantity of tissue destroyed, the tempo of its destruction and the individual reactivity of the mesodermal structures, Schilder's disease and diffuse encephalitis show no great differentiation. The destructive process attacks the most vulnerable structures first and with the greatest intensity. Other structures, the axons for example, are attacked secondarily, not as a result of myelin sheath damage, but because the process has extended. Other reasons for specificity of

4. Gasul, B.: Schilder's Disease (Encephalitis Periaxialis Diffusa): A Review of the Literature and Report of a Case, *Am. J. Dis. Child.* **39**:595 (March) 1930.

5. Globus, J., and Strauss, I.: Progressive Degenerative Subcortical Encephalopathy, *Arch. Neurol. & Psychiat.* **20**:1190 (Dec.) 1928.

6. Schaltenbrand, G.: Encephalitis Periaxialis Diffusa, *Arch. Neurol. & Psychiat.* **18**:944 (Dec.) 1927.

7. Bouman, L.: Encephalitis Periaxialis Diffusa, *Brain* **47**:453, 1924.

degree of damage have yielded no good evidence. Before the glia is attacked, and that usually at the very last, progressive forms appear only to degenerate finally, hence the lack of glial sclerosis, the appearance of gemästete glia or, in more advanced or more rapidly developing lesions, the status spongiosus.

The etiologic status of the diffuse encephalitides, including Schilder's disease, has not been solved after many years of pathologic study. No adequate criteria for not considering them infectious in origin and searching for their bacterial cause have been advanced by neuropathologists. Our case showed by all criteria a dissociation of what has been presumed to be toxic degenerative softenings without signs of inflammation and a diffuse perivascular inflammatory reaction. Certainly such a picture cannot be interpreted as meaning infection or degeneration if the present-day pathologic conclusions as to what causes the changes in either type are correct.

The newly discovered prevalence of cowpox encephalomyelitis has been startling in Holland, England and Germany. Cases have occurred about thirteen days after vaccination, usually in older children who have never been vaccinated before. The clinical syndrome simulates tetanus closely, and it is not improbable that this diagnosis was made before encephalitis became prevalent.

The pathologic observations have been typical for all cases. Multiple perivascular lesions are found, particularly about the venules, consisting of complete or incomplete softenings or, in the milder cases or younger areas, demyelination with relatively less axonal destruction. The lesions seem to have a predilection for white matter of both the spinal cord and the cerebrum. A relatively moderate mesodermal reaction in the form of perivascular lymphocytic infiltration has been noted. There seems to have been very little variation in the fatal cases studied in whichever country they arose. The identity of the pathologic reports of Bouman and Bok<sup>8</sup> from Holland, Perdrau<sup>9</sup> from England, Wilson and Ford,<sup>10</sup> and Hassin and Geiger<sup>11</sup> in this country is striking.

Many theories have arisen as to the etiology of this disease. The conception of a toxic degenerative disease was quickly abandoned in spite of the fact that the disproportionate destruction of the myelin

8. Bouman, L., and Bok, S.: Die Histopathologie der Encephalitis Post Vaccinationem, *Ztschr. f. d. ges. Neurol. u. Psychiat.* **111**: 495, 1927.

9. Perdrau, J. R.: The Histology of Postvaccinal Encephalitis, *J. Path. & Bact.* **31**: 17, 1928.

10. Wilson, R. E., and Ford, F. R.: The Nervous Complications of Variola, Vaccinia and Varicella with Report of Cases, *Bull. Johns Hopkins Hosp.* **40**: 337, 1927.

11. Hassin, G. B., and Geiger, J. C.: Postvaccinal (Cowpox) Encephalitis: A Clinicopathologic Report of a Case, *Arch. Neurol. & Psychiat.* **23**: 481 (March) 1930.

sheath and of the axons and the paucity of inflammatory cells resembled the observations in multiple sclerosis. The absence of a gliosis, for practically no astrocytic proliferation is stimulated, and the perivascular site of the lesions easily differentiates them from multiple sclerosis. Only recently, Hassin, who believed in the toxic degenerative causation of multiple sclerosis,<sup>12</sup> concluded that the pathogenesis of encephalitis following the use of cowpox vaccine is an exotoxin conveyed by the vaccine lymph.

Arguments for an identity of the disease with epidemic encephalitis seem rather feeble. In Holland, the high point of both types of cases has been in March, and there have been local epidemics of the vaccine cases. Levaditi, Nicolau and Bayarri<sup>13</sup> upheld this view, but they failed to offer adequate proof or to explain the extreme divergence of both clinical and pathologic observations in the disease. Epidemic encephalitis produces widespread parenchymatous damage particularly to nuclear structures, without foci and with severe mesodermal reactions.

The conception has arisen that vaccine encephalitis is due to some unknown latent virus harbored in the body of the vaccinated person and stimulated to activity by the vaccination. This view was strongly supported by Pette,<sup>14</sup> who believed that even finding the vaccine virus in the brain of a patient dying after vaccination, as in Aldershoff's<sup>15</sup> cases, does not prove that the causative virus is that of vaccinia unless it produces the typical pathologic conditions in the animal to which it is transmitted. He reported an analogous experiment in rabbits, cultivating *Bacillus bipolaris*, the organism of rabbit septicemia, in rabbits dying after vaccination. The vaccination merely stimulated the organisms latent in the animal's upper respiratory tracts to activity. Paschen,<sup>16</sup> after stating that vaccine strains which had not been neurotropic in Switzerland, Spain or Japan, when used in Holland produced encephalitis, found that the encephalitis thus produced may be counteracted by an injection of serum from a newly vaccinated person. Hurst and Fairbrother<sup>17</sup> have recently produced vaccinia infections in brains

12. Hassin, G. B.: Studies in the Pathogenesis of Multiple Sclerosis, Arch. Neurol. & Psychiat. **7**:589 (May) 1922.

13. Levaditi, Nicolau and Bayarri: L'étiologie de l'encéphalopathie post-vaccinale, Presse méd. **35**:161, 1927.

14. Pette, H.: Das Problem der post-vakzinalen Enzephalitis, München. med. Wchnschr. **75**:207, 1928.

15. Aldershoff, H.: Experimental Studies on a Case of Encephalitis Post Vaccinationem, Acta path. et microbiol. Scandinav., 1930, supp. 3, p. 9.

16. Paschen, E.: Postvaccinal Encephalitis: Pathogenesis and Prophylaxis, Deutsche med. Wchnschr. **56**:219, 1930.

17. Hurst, E. W., and Fairbrother, R. W.: Experimental Vaccinal Encephalitis in the Monkey and the Rabbit with Special Reference to the Problem of Encephalitis Following Vaccination in Man, J. Path. & Bact. **33**:463, 1930.

of monkeys, but have found pathologic changes indicative of a meningo-encephalitis very unlike that in human postvaccinal cases.

McIntosh,<sup>18</sup> who probably saw the first pathologic material of vaccine encephalitis and who has been studying the problem for years, has been able to develop a neurotropic strain of vaccinia by repeated passage through rabbits, which he can isolate from the brain. The brains of his experimental animals show changes similar to the pathologic vaccinal conditions that he found in human cases. McIntosh and Scarff<sup>19</sup> have lately reiterated the similarity of the changes in the brains in the experimental vaccinia encephalitis of animals and in the human type. They have also been able to transmit the virus from human to animal material, as Aldershoff did after them. Thompson,<sup>20</sup> however, was unable to modify his virus to secure an infection of the brain. Eckstein and Herzberg<sup>21</sup> isolated a virus from the blood of vaccinated persons on the eighth day and from the spinal fluid only in cases of encephalitis. They stated that it is known that vaccinia is a generalized disease in which the virus permeates all of the organs, except probably the brain owing to the choroid plexus barrier; when that breaks down the vaccinia permeates even the nerve tissue, causing encephalitis.

The problem becomes more difficult when one finds that rabies vaccine occasionally produces lesions, as described by Bassoe and Grinker,<sup>22</sup> typically the same as cowpox vaccine. Higier<sup>23</sup> also reported a fatal case of human rabies with an ascending course and lesions as in vaccinated patients. Spiller,<sup>24</sup> in 1903, studied a case of smallpox with again the identical pathologic processes, and recently Troup and Hurst<sup>25</sup> have reported a fresh case. Furthermore, Wohlwill<sup>26</sup> and Musser and Hauser,<sup>27</sup> in 1928, and others after them

18. McIntosh, J.: Encephalomyelitis in Virus Infections and Exanthemata: An Experimental and Pathological Study, *Brit. M. J.* **2**:334, 1928.

19. McIntosh, J., and Scarff, R. W.: The Reaction of the Central Nervous System to Vaccinia Virus, *J. Path. & Bact.* **33**:483, 1930.

20. Thompson, R.: Attempted Production of Vaccinal Encephalitis in Rabbits with a Testicular Virus, *Proc. Soc. Exper. Biol. & Med.* **26**:559, 1929.

21. Eckstein, A., and Herzberg, K.: Klinisch-experimentelle Untersuchungen über die Vakzinationsenzephalitis, *Deutsche med. Wchnschr.* **57**:264, 1930.

22. Bassoe, P., and Grinker, R.: Human Rabies and Rabies Vaccine Encephalomyelitis, *Arch. Neurol. & Psychiat.* **23**:1138 (June) 1930.

23. Higier, H.: Akute aufsteigende Landry'sche Paralyse im verlauf von Lyssa humana, *Ztschr. f. d. ges. Neurol. u. Psychiat.* **12**:353, 1912.

24. Spiller, W. G.: A Report of Two Cases of Paraplegia Occurring in Variola, *Brain* **26**:424, 1903.

25. Troup, A. G., and Hurst, E. W.: Disseminated Encephalomyelitis Following Small-Pox, *Lancet* **1**:567, 1930.

26. Wohlwill, F.: Ueber Encephalomyelitis bei Masern, *Ztschr. f. d. ges. Neurol. u. Psychiat.* **112**:20, 1928.

27. Musser, J. H., and Hauser, G. H.: Encephalitis as a Complication of Measles, *J. A. M. A.* **90**:1267 (April 21) 1928.

published studies on measles encephalitis that demonstrated again an identical pathologic process. Finally, Perdrau and Pugh<sup>28</sup> have found the same pathologic conditions in the distemper of dogs. Thus it seems that a variety of clinical conditions, including vaccination against smallpox or rabies and exanthematous diseases, such as measles and smallpox in human beings, produce an identical pathologic condition.

In case 1, without vaccination or exanthematous disease, with the clinical course of a rapidly progressing disseminated encephalomyelitis, there were the same characteristic pathologic features as in the others. In comparing the lesions in this case with those in our case in which rabies vaccine was used, we can find no difference. Are we dealing with an identical virus stimulated to activity by a variety of precipitating causes, or have we many specific but similar viruses evoking the identical biologic reaction in the host?

Discussion of cases 3 and 4 brings up the long repeated controversy as to the relation of multiple sclerosis to disseminated encephalomyelitis and its pathogenesis. To classify these two groups is as difficult as to divide Schilder's disease into degenerative and inflammatory forms, although it has frequently been attempted. The so-called acute multiple sclerosis has complicated matters. Although it proceeds with a rapid clinical course and a febrile reaction, the pathologic observations closely resemble those in multiple sclerosis in regard to the distribution and details of the foci. These are not related to a specific blood supply; the myelin sheaths are early and most severely damaged, and there is a progressive glial reaction and early gliosis. Differing from the chronic cases, there is greater axonal destruction and greater inflammatory reaction, so that Anton and Wohlwill<sup>29</sup> considered the acute and chronic cases distinct anatomic entities. They believed that the acute type is an encephalitis, but the chronic type a degenerative disease.

Jakob<sup>30</sup> has repeatedly expressed the view that the lymphocytic infiltration in the acute cases signifies an infection. Pette<sup>31</sup> considered

28. Perdrau, J. E., and Pugh, L. P.: The Pathology of Disseminated Encephalo-Myelitis of the Dog (the "Nervous Form of Canine Distemper"), *J. Path. & Bact.* **33**:79, 1930.

29. Anton, G., and Wohlwill, F. R.: Multiple nicht-eitrige Enzephalomyelitis und multiple Sklerose, *Ztschr. f. d. ges. Neurol. u. Psychiat.* **12**:31, 1912.

30. Jakob, A.: Ueber diffuse infiltrative Enzephalomyelitis in ihren Beziehungen zur diffusen und multiplen Sklerose mit besonderer Berücksichtigung der infektiös-entzündlichen Genese, *Neurol. Centralbl.* **33**:590, 1914; Zur Pathologie der diffusen infiltrativen Enzephalomyelitis in ihren Beziehungen zur diffusen und multiplen Sklerose, *Ztschr. f. d. ges. Neurol. u. Psychiat.* **27**:290, 1915.

31. Pette, H.: Ueber die Pathogenese der multiplen Sklerose, *Deutsche Ztschr. f. Nervenhe.* **105**:76, 1928; Zur Frage der infektiösen Aetiologie der akuten disseminierten Enzephalo-myelitis respektive der akuten multiplen Sklerose, *München. med. Wchnschr.* **74**:1409, 1927.

both types as infectious. His conception of a primary parenchymatous damage as indicative of a virus infection has been vigorously attacked by Spielmeier. Turnbull<sup>32</sup> expressed the belief that acute and chronic forms of multiple sclerosis are incapable of pathologic distinction, and that they can be termed infectious, but are sharply differentiated from the postvaccinal type of encephalitis which has a characteristic pathology. Spiller<sup>33</sup> considered that there is no difference between disseminated encephalomyelitis and acute multiple sclerosis. Dawson<sup>34</sup> thought that the lesions were associated with terminal blood vessels, and that they were due to toxins brought by the blood stream. Hassin always contended that multiple sclerosis is a toxic degenerative disease because of the early selective myelin sheath damage. He found evidences of this primary myelin condition distant from the main lesions.

It is thus apparent that a diversity of opinion exists as to what should be known as acute multiple sclerosis or acute disseminated encephalomyelitis. These seem to comprise a heterogeneous group. Aside from a variable mesodermal reaction, chronic multiple sclerosis is well defined pathologically, even though the interpretations of various authors may be different. In the acute cases one deals not only with cases showing a rapidly developing demyelination, nerve fiber damage and gliosis, but also with others showing inflammatory softenings in which the entire tissue is softened and which is secondarily scarred with connective tissue as in our case 3.

A form of acute brain reaction has been described in adults and children that has been termed toxic.<sup>35</sup> This type is found secondary to an endogenously formed toxin, either bacterial or protein, and resembles closely acute lead poisoning. The changes in the brain are not due to the invasion of the nerve tissue by organisms but by their toxins. There is a characteristic profound change in the capillary endothelium with secondary parenchymatous disturbances, particularly of the ganglion cells, although they may be primarily damaged as well. Epidemic encephalitis has been termed by some a toxic reaction secondary to influenza, although the pathologic process is so like that in rabies and Heine-Medin's disease, two diseases caused by a virus, as frequently to render pathologic differentiation impossible. It thus seems probable that epidemic encephalitis is also a virus disease.

32. Turnbull, H.: Encephalo-Myelitis in Virus Disease and Exanthemata, *Brit. M. J.* **2**:331, 1926.

33. Spiller, W. G.: Encephalomyelitis Disseminata, *Arch. Neurol. & Psychiat.* **22**:637 (Sept.) 1929.

34. Dawson, J. W.: The Histology of Disseminated Sclerosis, *Edinburgh M. J.* **17**:229, 1916.

35. Grinker, R. R., and Stone, T. T.: Acute Toxic Encephalitis in Childhood, *Arch. Neurol. & Psychiat.* **20**:244 (Aug.) 1928.

If a pathologic classification of the central nervous infections were to be proposed on the basis of distinct, regularly occurring microscopic changes, it is apparent that each group would embrace examples of more than one clinical syndrome. Exclusive of syphilis, the parasitic infections and the changes in the brain in sepsis, with its miliary abscesses, such a classification of nonsuppurative encephalitides would be as follows:

1. Severe focal demyelination, less severe axonal damage, microgliosis, mild or absent perivascular lymphocytic infiltration, gliosis (chronic multiple sclerosis and certain cases of acute multiple sclerosis).
2. Focal lesions of incomplete or complete softenings, not perivascular, microgliosis, varying degree of lymphocytic infiltration, vascular proliferation and connective tissue scar formation (acute disseminated encephalomyelitis and certain cases of acute multiple sclerosis).
3. Focal perivascular incomplete softenings involving the whole nerve fiber, coalescing of lesions to form softenings, microgliosis, mild lymphocytic reaction, secondary gliosis (cowpox and rabies vaccine, measles, varicella and variola, and certain cases of disseminated encephalomyelitis).
4. Diffuse subcortical destruction of nerve fibers, probably beginning in the myelin sheaths, mild or absent lymphocytic infiltration, primary progressive gliosis with secondary regressive glial forms, connective tissue scar (Schilder's disease and disseminated encephalitis).
5. Diffuse but relatively selective (basal nuclei, medulla or anterior horn cells) ganglion cell destruction, abundant perivascular and tissue lymphocytic infiltration, mild microgliosis, white matter spared (rabies, epidemic encephalitis and Heine-Medin's disease).
6. Hyperplastic meningeal reaction, regressive changes in capillary endothelium, formation of new blood vessels, degenerative changes of ganglion cells, absent mesodermal infiltrations (toxic encephalitis secondary to acute infections and exogenous toxins such as lead).

Examining this pathologic classification with the view of determining which are true infections, one is struck with the fact that group 5 contains three clinical types, two of which are proved virus diseases, and that microscopically all are with difficulty differentiated, and then only by the knowledge of the location of the most severely damaged tissue and by corroborative clinical data. On the other hand, group 6 is definitely noninfectious, because the changes found are identical with other toxic states, as, for example, heavy metal poisons.

All of the other types are of doubtful etiology, and, curiously, all tend to be focal in distribution and to attack mostly the white matter. What criteria should one use to determine if possible whether these

focal diseases are infectious? The rôle of the perivascular infiltrations of lymphocytes and plasma cells seems to have been given an important part in designating an infectious disease by most neuropathologists.

The central nervous system does not possess a connective tissue stroma except that found in the walls of the blood vessels. This vascular reticulin is frequently proliferated locally in the diseases under discussion and enmeshes perivascularly situated gitter cells. The vascular endothelium also is stimulated into proliferation and new blood vessel formation may result. But, as Bailey and Schaltenbrand<sup>36</sup> have shown, the vascular connective tissue invades the nerve tissue only when the pia-glia membrane is broken. This occurred in case 3, in which reticulin freely entered into a scar formation.

The glia tissue is profoundly altered in these cases. Almost always there is an early macrogliosis of variable degree. Frequently in multiple sclerosis the noxa is not strong enough to destroy, or it is not directed against the proliferated glia so that a gliosis occurs which persists and increases after the activity of the disease has subsided. Studies of pure vascular occlusions have shown that the glia, of all the tissue components, is most resistant to destruction. In Schilder's disease the noxa attacks the glia after the nerve fibers are destroyed, and the initially proliferated glia undergo marked regressive changes (*gamästete Glia*). In certain cases of disseminated encephalomyelitis the glia cells are destroyed early in the complete softenings.

The microglia cells are quickly stimulated to proliferation and rapidly form gitter cells and scavenge lipoids resulting from nerve fiber and sheath destruction. Spielmeyer's special glial reaction, which he pictured as mobile glia loosed from the glia reticulum to form glia nests, is undoubtedly microglia. He spoke of a gliogenous reaction to infection. By a criterion such as the ability to pick up particulate matter these microglia, which arise from mesoderm, must be considered as part of the reticulo-endothelial system. Their function is apparently not only that of scavenger cells as their great numbers, their tendency to form "Rasen" and their ability to engulf bacteria and to wall off lesions would indicate.

Parenchymatous changes in ganglion cells, myelin sheaths and nerve fibers are the results of the fundamental process and do not qualify its nature, except to help in differentiating the noxious agent which seems characteristically to attack either gray or white matter, although in no case does it attack one type exclusively. The progression of damage from sheath to nerve fiber should be considered as a quantitative matter. No disease of the central nervous system attacks

36. Bailey, P., and Schaltenbrand, G.: Die perivaskuläre Piagliamembran des Gehirns, *J. f. Psychol. u. Neurol.* **35**:199, 1928.

the nerve fiber first; its covering must first or simultaneously be destroyed, but the axon may exist without its sheath. The presence of demyelination with preserved fibers offers no help in the determination of the infectious or degenerative character of the lesion.

In the central nervous system there is then a syndrome of inflammation to infections which consists in local changes in the vascular endothelium, vascular connective tissue, true glia and microglia. Such are the possible local tissue reactions to infection. Their reactivity and the selective damage of the noxious agent in the parenchyma and in the reacting elements themselves constitute the microscopic evidence of reactivity of the whole organ involved. But added to these local factors there may be hematogenous elements partaking in the inflammatory process. Lymphocytes, leukocytes or plasma cells may appear in the perivascular spaces or penetrate the tissue, adding another evidence of inflammation. But these infiltrations are only one part of the whole picture and, possibly, from what is known of the pia-glia vascular barrier, play an insignificant rôle in defense. One should therefore stress the importance of such hematogenous elements less, and consider more the entire pathologic syndrome. When we do so it is obvious that there is no adequate reason for considering any of the diseases outlined as primarily degenerative except group 6.

The pathologic picture gives no clue as to the nature of the disease in groups 1 to 4. In every example, evidences of inflammation are obvious if one realizes the broad meaning of the term. It is impossible to differentiate primary inflammation from that secondary to tissue destruction. The solution of the problem must come from the discovery of the etiologic agents, but from the pathology any etiologic conclusions are as yet unwarranted.

## ENCEPHALITIS AND ENCEPHALOMYELITIS IN MEASLES

A PATHOLOGIC REPORT OF SIX CASES \*

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Nervous complications following measles were known more than a century ago, but the first pathologic report (Barlow and Penrose<sup>1</sup>) dates from 1886. The authors described a case of paraplegia occurring a few days after the appearance of the measles rash. Histologically, the cord showed that the changes were entirely vascular. There was great enlargement of the vessels, most of the veins being many times their normal caliber and crammed with corpuscles. Many vessels were surrounded by a zone of coagulated exudation, and beyond this for a considerable distance the surrounding tissue was infiltrated with leukocytes, giving the appearance in transverse sections of cells in concentric rings.

Since then, other reports have appeared in the literature dealing with nervous complications of measles. Some authors have considered the clinical aspect of the disease and others the pathologic aspect. In some cases, lesions of both the brain and the spinal cord were present.

Up to the present, case reports from the pathologic standpoint are rather scarce, the most recent ones having appeared in the literature from 1923 to 1930. In 1923, Tinel and Benard<sup>2</sup> examined the cord of a man, aged 21, in whom ascending paralysis of the Landry type developed on the fourth day of the infection. The authors reported the presence of small areas of perivascular demyelination in both the gray and the white substance of the cord. The proliferative elements consisted of connective tissue cells and neuroglial elements.

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1. Barlow and Penrose: On a Case of Early Disseminated Myelitis, *Tr. Med.-Chir. Soc., London* **70**:77, 1887.

2. Tinel and Benard: Myélite aiguë ascendante au cours de la rubéole, *Rev. neurol.* **39**:310, 1923.

Bergenfeldt<sup>3</sup> (1924) described a case of myelitis as a complication of measles. The microscopic studies (Sjovall) disclosed the presence of perivascular collars of cells formed by small round elements and cells grouped around fat droplets. The fat was free or embedded in other cellular structures.

The case reported by Mosse and Creutzfeldt<sup>4</sup> (1926), one of pertussis complicated by measles, showed mental symptoms, which developed on the fourth day of the rash. Death occurred on the twelfth day. Histologically, a purely degenerative process was found mostly in the white matter of the cerebral convolutions. In the areas of degeneration, which were perivascular, there was destruction of the myelin sheaths and corresponding degenerative changes of the nerve fibers. The perivascular neuroglial elements, especially the astrocytes, were increased. Subpial and subependymal gliosis was present. Hyperplasia of the vascular endothelium was noticeable. The cortical lesions of pertussis described by Spatz and Neuburger were not present.

In the same year, Brock<sup>5</sup> and Siegmund reported the case of a child who became unconscious on the fifth day of measles and died twenty-three days later in coma. Microscopically, the lesions, which were diffuse in the entire brain, consisted in perivascular proliferation of neuroglial elements of the protoplasmic type. The myelin sheaths appeared destroyed, while the axis cylinders were little injured. No mesodermal reaction was reported.

In 1927, Reimold<sup>6</sup> described a case of encephalitis in measles in which, histologically, congestion, hemorrhages and proliferation of the walls of the blood vessels were reported. The final diagnosis was acute hemorrhagic cerebral encephalitis.

Stern<sup>7</sup> (1928) reported a case of the same condition in which inflammatory changes were diffuse in the cortex, basal ganglia, mesencephalon and brain stem. The spinal cord was not examined. The nature of the perivascular exudate was a mixture of gutter cells, glia cells and lymphocytes. In some places the infiltration was exclusively of lymphocytic nature, recalling the type of exudate seen in epidemic encephalitis.

3. Bergenfeldt, E.: Myelitis als Masernkompliation, *Acta med. Scandinav.* **61**:281, 1924.

4. Mosse and Creutzfeldt: Zwei Fälle von akuter Gehirnregeneration nach Masern, *Jahrb. f. Kinderh.* **62**:272, 1926.

5. Brock, J.: Ueber Systematik und Klinik der meningoencephalitischen Krankheitszustände im Kindersalter, *Ztschr. f. Kinderh.* **40**:552, 1925-1926.

6. Reimold, W.: Ueber encephalitische Syndrome im Verlaufe von Infektionskrankheiten, *Monatschr. f. Kinderh.* **37**:336, 1927.

7. Stern, W.: *Die epidemische Encephalitis*, ed. 2, Berlin, Julius Springer, 1928.

In the same year, Musser and Hauser<sup>8</sup> reported ten cases of encephalomyelitis in measles in which autopsy was performed. Microscopically, there was marked injection of vessels and capillaries. A general and diffuse parenchymal round cell infiltration was reported and, particularly around the blood vessels, many small hemorrhages were seen. Perivascular hemorrhages were also reported about some of the small vessels filling the perivascular spaces. No specific stains were used for histologic differentiation of the perivascular elements.

The patients in two cases reported by Wohlwill (1928) both died on the tenth day of measles, the first four days after the onset of the coma. The lesions reported in the first case consisted of perivascular proliferation of the small veins affecting the whole area of the cortex, basal ganglia, midbrain, cerebellum and other structures. The spinal cord, which was also examined in this case, showed the same type of lesion with the addition of marginal neuroglial proliferation. Corresponding to the neuroglial proliferation there was an acute degeneration of myelin sheaths and to a lesser extent of nerve fibers.

In his second case, Wohlwill reported also changes of the ganglion cells, from acute swelling to the severe type of lesions (*schwere Zellerkrankung*) of Nissl, which were especially pronounced in the spinal gray matter.

Wohlwill<sup>9</sup> also examined the brain and spinal cord in five cases of measles and pneumonia. In two of these no pathologic changes were found. In a third there was an unusually large number of glia rosetts in the white matter of the cord, showing no relation to the blood vessels. In the other two cases, a cerebral complication was present: in one an autogenic meningitis, in the other an extensive vein and sinus thrombosis. In the latter, perivascular proliferation of neuroglia was present recalling that described in the few original cases. However, since in this case the numerous static hemorrhages that occurred not only in the cortex but also in the cortical white matter showed also neuroglial proliferation, the author was in doubt as to the significance of the lesions in which there was perivascular neuroglial proliferation without hemorrhage.

In 1929, Greenfield<sup>10</sup> described the case of a girl, aged 6, who showed cerebral symptoms on the fifth day of the measles eruption and died forty hours later. The histologic examination revealed a considerable

8. Musser, J. H., and Hauser, G. H.: Encephalitis as a Complication of Measles, *J. A. M. A.* **90**:1267 (April 21) 1928.

9. Wohlwill, F.: Ueber Encephalomyelitis bei Masern, *Ztschr. f. d. ges. Neurol. u. Psychiat.* **112**:20, 1928.

10. Greenfield, J. G.: The Pathology of Measles Encephalomyelitis, *Brain* **52**:171, 1929.

perivascular infiltration with lymphocytes and plasma cells. A number of perivascular zones of demyelination were scattered through the brain and brain stem. No fat was present in the demyelinated areas outside the sheaths. The proliferating cells in the demyelinated areas were found by the Hortega stain to be microglia. The Bielschowsky method showed little destruction of nerve fibers in the demyelinated areas. There were no alterations in the nerve cells of the cortex or the basal ganglia. In his summary, the author concluded that encephalomyelitis in measles is characterized, from the histologic standpoint, by three main types of changes: (1) diffuse congestion of the brain, especially of the white matter, sometimes causing petechial hemorrhages; (2) a discrete perivascular infiltration with round cells (this is often absent); (3) small perivascular zones of demyelination. The last is the most characteristic change of this form of encephalomyelitis.

In the same year, Walthard<sup>11</sup> reported a case of encephalomyelitis that developed in the acute period of measles; the patient died after an illness of four and one-half weeks. A summary of his histologic observations is as follows: There was widespread perivascular glial proliferation, with marked destruction of the myelin sheaths and axis cylinders in the region of the centrum ovale of both hemispheres, and in the basal ganglia. In places, there was extensive glial proliferation, and in certain parts of the cortex and in the anterior horns of the cord, very slight perivascular round cell proliferation of isolated vessels. No subependymal glial proliferation was present, nor was the subpial zone in the cord described by Wohlwill found.

We have secured autopsy material in nine cases of patients who died of nervous complications in the course of measles infection. We shall report the pathologic changes in only six cases, the histology of which is characteristic for this type of disease. One of us (I. H. S.) has added a clinical summary to each of the six cases in the hope that it may prove useful to both clinicians and pathologists.

#### REPORT OF CASES

*CASE 1.—Clinical History.*—W. C., a boy, aged 7½ years, who was admitted to the hospital on March 28, 1930, had had mumps one year before, and pertussis two years before. Six days prior to admission there appeared a cough, fever, coryza and a macular rash that occurred first behind the ears and spread over the entire body. On the day prior to admission, the child became drowsy and lapsed into coma.

*Physical Examination.*—The patient was fairly well developed and poorly nourished; he was in a comatose state; the temperature was 103 F.; the pulse rate,

11. Walthard, K. M.: Spätstadium von Masernenzephalitis: Bemerkungen zur Histologie und Pathogenese der Masernenzephalitis, *Deutsche Ztschr. f. Nervenhe.* **111**:117, 1929.

112, and the respiratory rate, 24. At times he could be aroused by painful stimulation. There was a macular blotchy rash on the face, trunk and extremities. The face was flushed. At times he ground his teeth. The conjunctivae were injected, and episcleritis was present; the pupils were unequal in size, the right being somewhat dilated; both reacted sluggishly to light, the right more so than the left. The ears were normal. There was a slight discharge from the nose. The tongue was red and coated, the buccal mucosa was injected, and a few faded Koplik spots were present. The tonsils were hypertrophied and reddened. The uvula was in the midline; the pharynx was injected. There was no impairment to percussion; scattered râles were heard throughout both lungs. The heart sounds were clear and regular; no murmurs were present. There was marked distention of the bladder; on catheterization, 14 ounces of urine was removed. Palpation of the abdomen revealed no abnormality. The neck was rigid, and there were positive Kernig and Brudzinski signs. The left knee reflex was absent, and the right was diminished; the biceps, triceps and radial periosteal reflexes were absent, as were also the abdominal, cremasteric and palatal reflexes. There was a positive bilateral Babinski sign, which was more marked on the left than on the right. On scratching the inner surface of the left thigh, there was a convulsive twitch of the left leg and foot.

*Diagnosis.*—The diagnosis was encephalomyelitis in measles.

*Laboratory Data.*—Lumbar puncture on admission revealed clear cerebrospinal fluid under slightly increased pressure. Six cubic centimeters was removed for examination. Cytology revealed: a "large increase in the number of cells," all of which were mononuclear leukocytes; no organisms in a stained smear; albumin, +; globulin, +; dextrose, +++; cultures, negative.

Urinalysis of a catheterized specimen showed: amber color; clear fluid; specific gravity, 1.026; reaction, acid; albumin, none; sugar, none; acetone, a trace. Microscopic examination gave negative results.

*Course.*—The patient was dehydrated and had apparent difficulty in swallowing. Four hundred cubic centimeters of physiologic solution of sodium chloride was given by hypodermoclysis.

March 29: The condition was the same as on admission. As the patient failed to void urine, catheterization was done, and 8 ounces of urine removed.

March 30: The respiration was labored, and many coarse râles were heard through the lower lobes of both lungs posteriorly, more markedly on the left side. The patient's general condition was poor, and he was considerably dehydrated. Fluids were administered by hypodermoclysis. Otoscopic examination revealed: right drum, red; landmarks obliterated; left drum, normal in appearance. A blood count revealed: white cells, 14,800 per cubic millimeter; 78 per cent polymorphonuclears, 20 per cent lymphocytes and 2 per cent large mononuclears.

March 31: The child was moribund. The respiration was labored, and many moist bubbling râles were heard throughout both lungs. The heart sounds were rapid and weak. The abdomen was soft, and no palpable masses were present. On both lower extremities there were several large purpuric areas the size of a fifty cent piece. The rest of the surface of the skin still showed a fading macular rash. The bladder was catheterized. The urine was clear, with a specific gravity of 1.024; it was acid; no albumin, sugar, acetone or diacetic acid was present; microscopic examination gave negative results. The white blood cells numbered 45,000 per cubic millimeter, of which 91 per cent were polymorphonuclears and 9 per cent lymphocytes. The patient died during the evening.

*Histologic Study.*—The meninges appeared considerably congested, the blood vessels being filled with red blood cells. Here and there were small hemorrhages, partly due to diapedesis and partly to vascular rupture. Red blood cells were found between the various layers of blood vessels, in the perivascular spaces and in the surrounding tissue. No trace of exudate was seen.

The brain tissue was considerably hyperemic, the veins being especially congested (fig. 1). Here and there were some red thrombi, as will be seen in figure 1. The lamination of the cortex grossly was well preserved, but here and there was disturbed through the accumulation of proliferated elements. These elements were either free in the tissue between the nerve cells, or surrounding the blood vessels, especially the veins. More characteristic was the appearance of the white

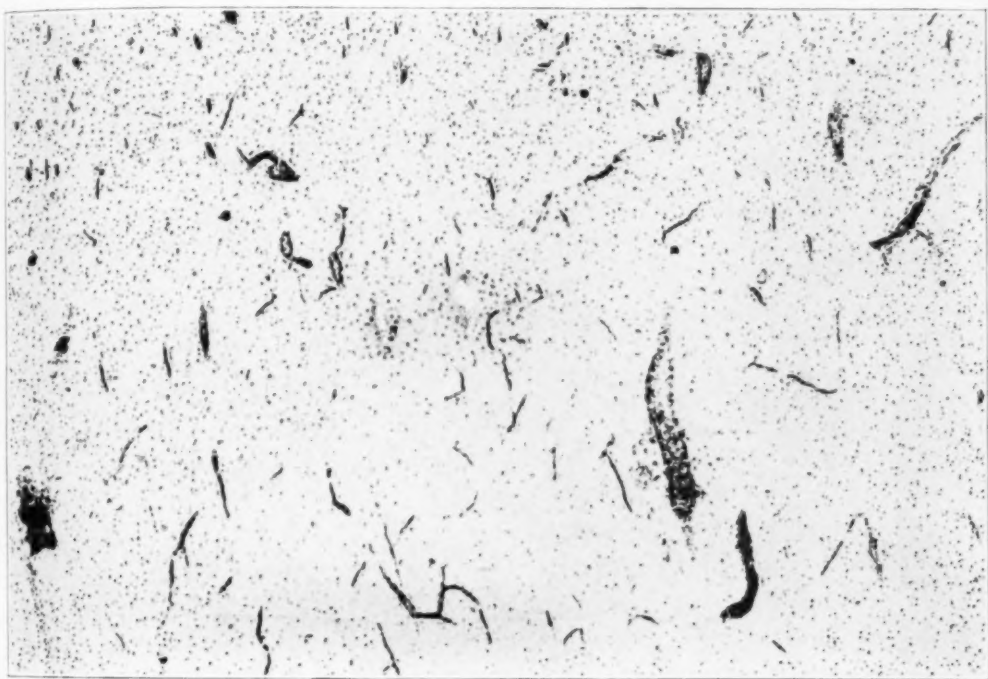


Fig. 1.—Considerable congestion and presence of small red thrombi. Bielschowsky-Plein method.

substance, in which a considerable accumulation of proliferated elements was spreading freely into the tissue but more consistently surrounding the blood vessels (fig. 2). The perivascular proliferation formed numerous foci of various sizes, which were scattered throughout the white substance. Some of the foci had a tendency to fuse, forming large areas in which proliferated elements were pressed together surrounding a group of two or more blood vessels. The elements of the proliferation appeared with the usual stains (hematoxylin-eosin and Nissl) as elements the nuclei of which were somewhat elongated and lobulated (fig. 3A). The cytoplasm was somewhat enlarged and in some instances very abundant. These cells did not recall lymphocytes or plasma cells. With appropriate methods of silver impregnation we have been able to prove beyond doubt that most of

them belong to the group of the so-called microglia cells. Figure 3 *B* shows in a convincing manner the nature of these proliferated elements. Under a higher power, no doubt arises as to the category of cells forming the perivascular proliferation (fig. 4 *A*). It is important to point out that while in figure 4 *A* most

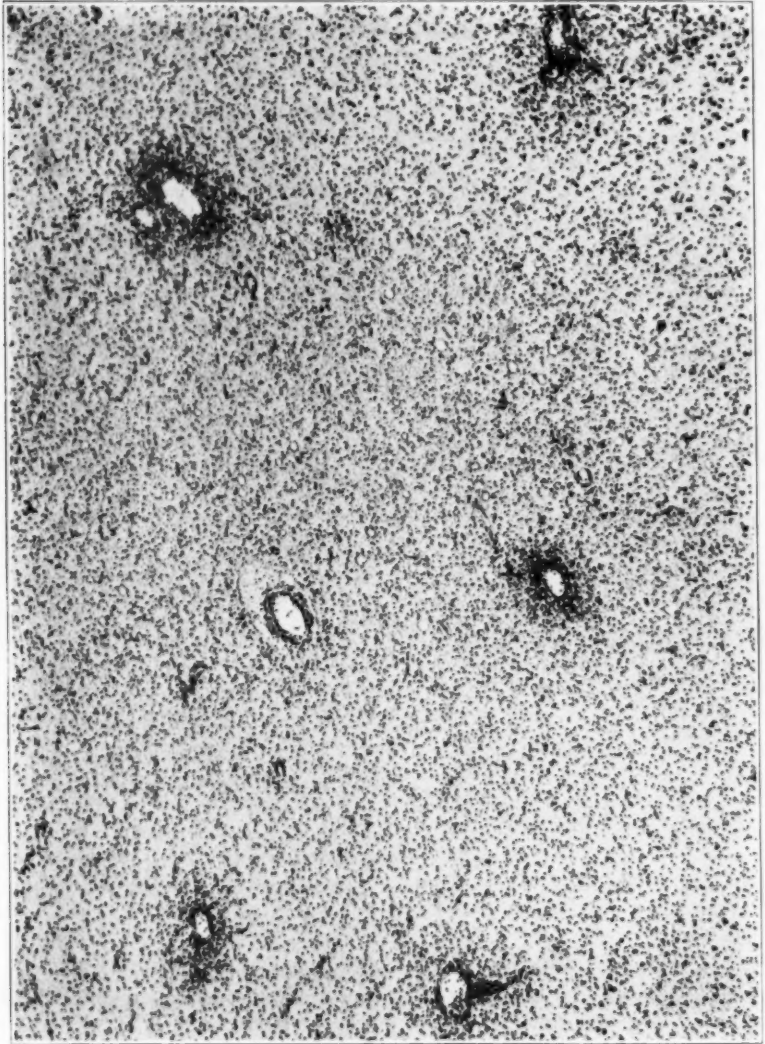


Fig. 2.—Diffuse perivascular proliferation in the white substance. Nissl stain.

of the elements have an elongated aspect recalling the so-called rod cells, in other instances the same cells show a definite transformation into larger elements up to compound granular corpuscles (fig. 4 *B*).

The condition of the nerve cell varied from area to area, and there was undoubtedly an involvement that was leading to their disappearance. The lesions

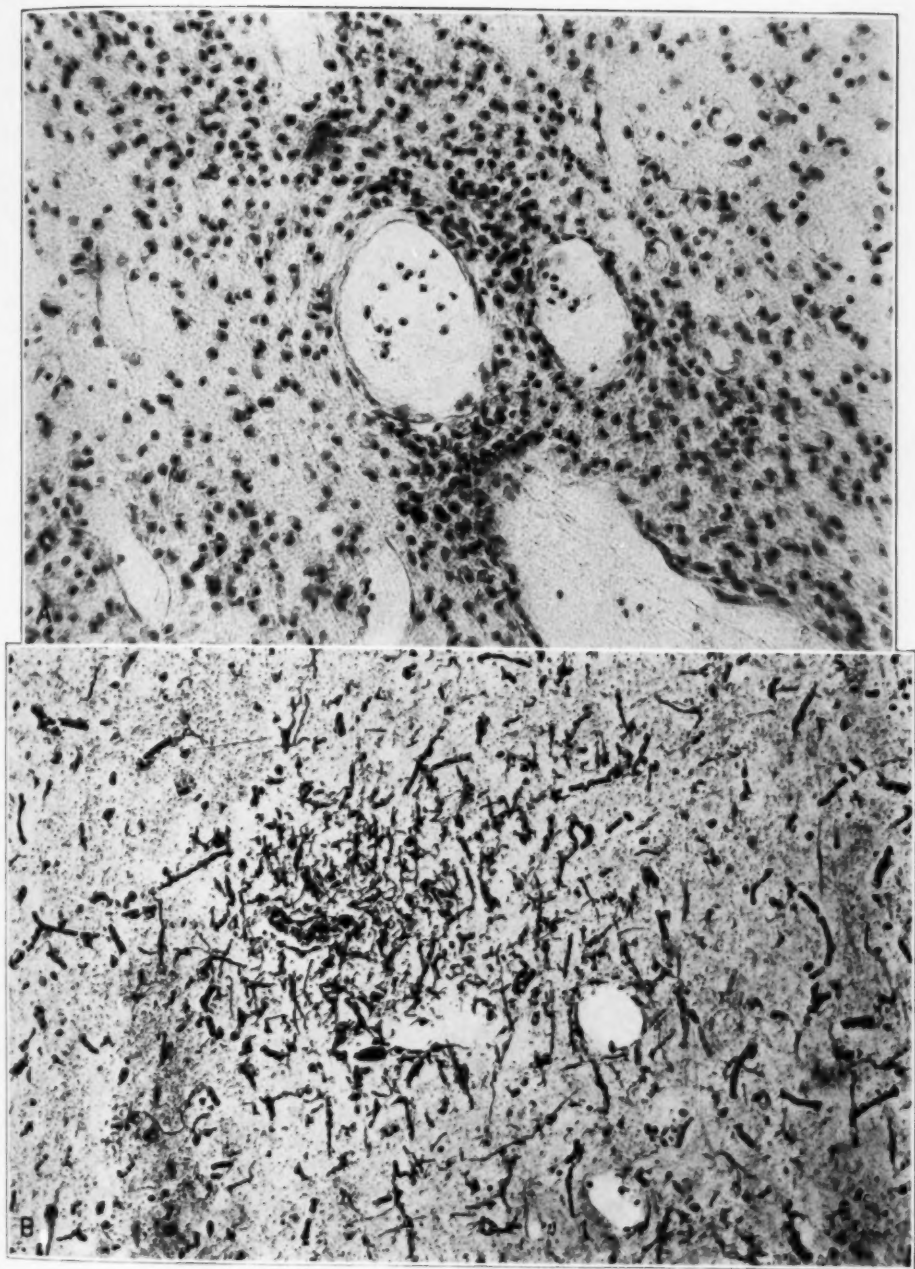


Fig. 3.—*A* shows the details of the perivascular proliferation, showing cells with deformed and elongated nuclei. Hematoxylin and eosin stain. *B* shows a special stain of the perivascular proliferation, showing that the cells are formed mainly by microglia cells. Hortege silver carbonate method (Globus-Penfield modification).

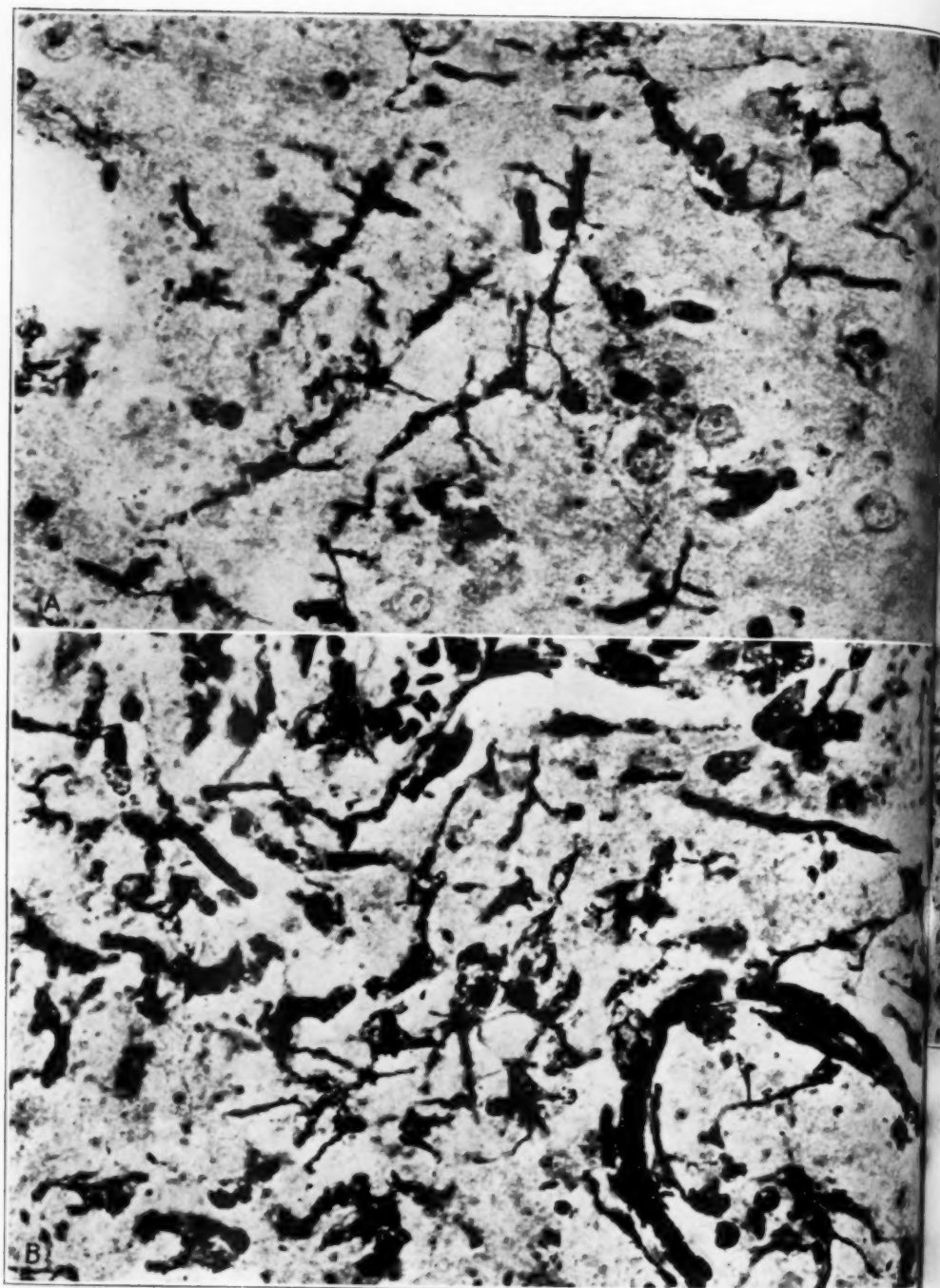


Fig. 4.—*A* shows the hypertrophic microglial element forming the bulk of the perivascular proliferation. Hortega silver carbonate method (Globus-Penfield modification). *B* shows the details of an area of perivascular proliferation, illustrating the transformation of some of the microglia into compound granular corpuscles. Hortega silver method (Globus-Penfield modification).

varied from an acute swelling to the most severe type of lesion described by Nissl as liquefaction. Here and there the degenerative process in the cortex was less pronounced and the nerve cells seemed to fade out gradually, leaving at times a shadow of their previous structure. At other times, the disappearance of a number of cells was manifest under the appearance of acellular areas in which some of the disintegrating elements were still visible (fig. 5). It is important to point out that here and there nerve cells were seen suffering from ischemic changes consisting in shrinkage of the cell body, disappearance of the Nissl granules and deformity of the nucleus.

The astrocytes participated in the reaction of the tissue by progressive and regressive changes. Among the progressive changes were the protoplasmic and



Fig. 5.—Cortex, showing proliferated cells scattered in the various layers of the region and a large patch where the cells are considerably diminished in number. In this area some of the cells are seen gradually disintegrating. Nissl stain.

fibrous types of hypertrophy. The protoplasmic reaction was especially seen in the perivascular area where the elements showed an enlarged cytoplasm. Some of the elements underwent later regressive changes represented by clasmotodendrosis and disintegration of the astrocytes. The fibrous type of reaction was seen somewhat distant from the perivascular areas and consisted especially of hypertrophy of the body and processes of the astrocytes.

Preparations for myelin sheaths disclosed the presence of numerous patches of demyelination that occurred generally as perivascular areas (fig. 6 *A*). Under

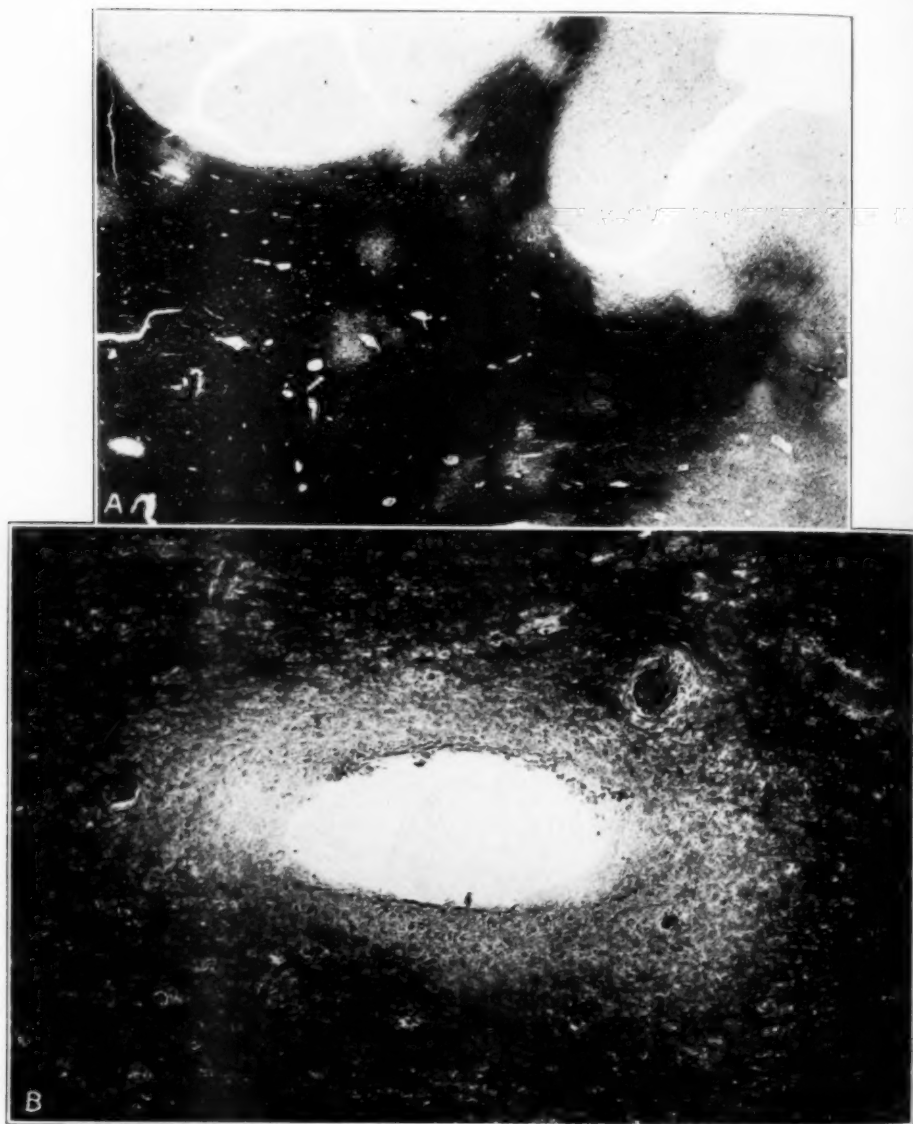


Fig. 6.—*A* shows multiple areas of demyelination, giving to the tissue a moth-eaten appearance. Spielmeier's method for myelin sheaths. *B* shows the details of a perivascular area of demyelination, showing the disappearance of most of the myelin sheaths and the occurrence of disintegrated granular-like material. Spielmeier's method for myelin sheaths.

a higher power lens, the clear areas surrounding the blood vessels were seen to correspond to demyelination represented by the breaking down of the myelin sheaths into fragments or granules and their gradual disappearance (fig. 6 B).

Correspondingly, the nerve fibers suffered in the same perivascular area. All the phases of degenerated neurofibrils were also encountered, from the swelling of the axons to their fragmentation in small granules (fig. 7). The involvement of the myelin sheaths and of the axis cylinders was not localized only in the perivascular areas, but was encountered, though to a lesser extent, in more distant areas. The proliferative elements, although more pronounced in the perivascular areas, were encountered here and there as free collections in the surrounding tissue. It is true that in serial sections we often found the relation of the proliferation to a blood vessel, but a certain amount of proliferation undoubtedly occurred independent of any definite connection. At the boundaries

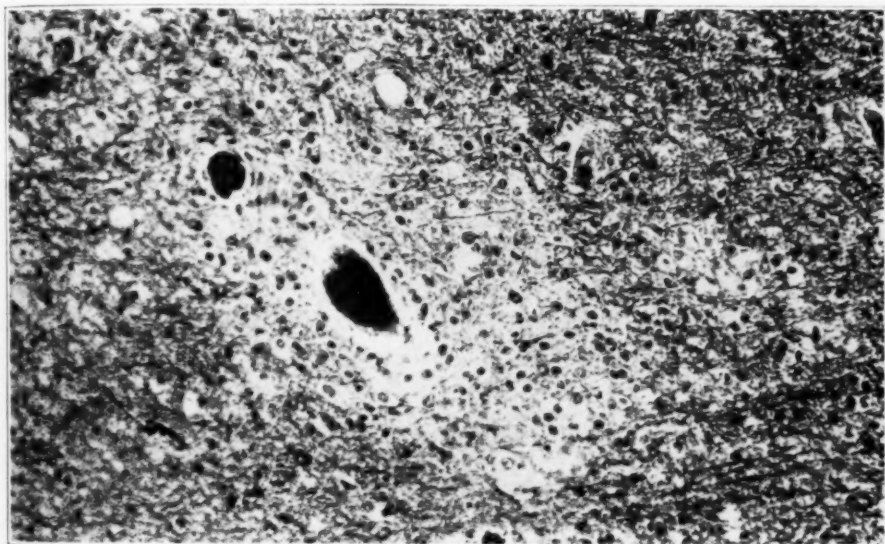


Fig. 7.—Considerable destruction of the axis cylinders in a perivascular demyelinated area. A few neurofibrils are still seen crossing the involved area. Bielschowsky stain for neurofibrils.

between gray and white matter there was a tendency of the proliferated elements to collect in a more conspicuous manner.

The pathologic process was diffused through all areas of the brain. There was, however, a certain predominance of the lesion in the occipital and frontal areas. Although the lesions were more pronounced in the white matter, gray structures were involved, as for instance the basal ganglia in which the proliferation was manifest in both the thalamus and the lenticular nucleus. The internal capsule was also considerably involved. In the mesencephalon, the perivascular proliferation was considerably marked in the surroundings of the red nucleus and in the dorsal limits of the substantia nigra. In the pons the lesions were very severe and seemed to affect by predilection the pontile nuclei, while the involvement of the transverse fibers and pyramidal tracts was much less conspicuous. In

the medulla oblongata, beside diffusion of the same fundamental process, there was a definite marginal, as well as a subependymal, proliferation all along the floor of the fourth ventricle. This proliferation was of the same nature as that involving the blood vessels, mostly represented by neuroglial and microglial hyperplasia. In the cerebellum, the characteristic proliferation involved mainly the white substance and the region of the dentate nucleus, respecting to a large extent the lamina molecularis and the lamina granularis (fig. 8). Unfortunately, the spinal cord was not available for study, and no report concerning it can be included.

CASE 2.—*Clinical History*.—R. D., a girl, aged  $3\frac{1}{2}$  years, who was admitted to the hospital on April 9, 1930, had had varicella one month previously. The illness began, five days prior to admission, with coryza and conjunctivitis. A rash

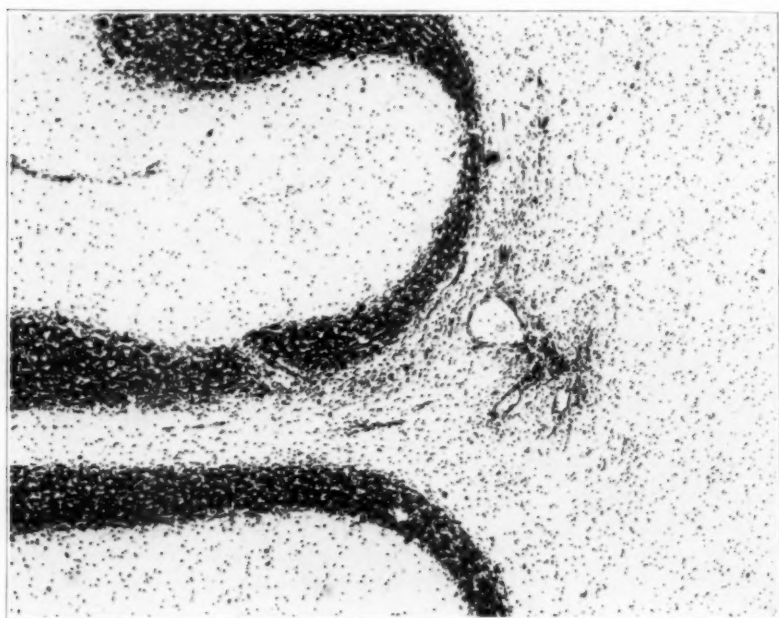


Fig. 8.—Perivascular proliferation in the white substance of the cerebellum contrasting with the relative integrity of the cortical layers. Nissl stain.

appeared on the face and body on the following day. On the day prior to admission, the child became drowsy and later in the day had generalized convulsions.

*Physical Examination*.—The patient was fairly well developed and nourished and was in a comatose condition. The temperature was 100 F.; the pulse rate, 140, and the respiratory rate, 20. There was a fading macular rash on the face and body, which looked like a fading measles rash. There was a marked conjunctivitis; the pupils were equal in size and reacted to light. The ears were normal. There were aphthous patches on the buccal mucosa of the mouth; the tongue was coated; the palate showed a normal arch; the pharynx was injected. In the lungs, the sounds were clear on auscultation and percussion. The heart rate was accelerated; the sounds were clear, and no murmurs were heard. The abdomen was soft; no masses were palpable. There was marked rigidity of the neck, and positive Kernig and Brudzinski signs were elicited on the left side; the

knee reflex was exaggerated on the left and present on the right; a positive Babinski sign was present on the left. The abdominal reflexes were diminished on the right and absent on the left; the biceps and triceps reflexes were diminished.

*Diagnosis.*—The diagnosis was encephalitis in measles.

*Laboratory Data.*—Lumbar puncture on admission revealed clear cerebrospinal fluid under normal pressure; there were 68 cells per cubic millimeter, all mononuclear; no organisms were seen on direct smear; albumin reactions were +; the globulin, +, and the dextrose, +++; cultures were negative. The blood count showed: red cells, 4,200,000 per cubic millimeter; hemoglobin, 75 per cent; white cells, 15,400; 91 per cent polymorphonuclears, 6 per cent lymphocytes and 3 per cent basophils. Urinalysis showed: urine, acid; specific gravity, 1.024; albumin, ++; sugar, acetone and diacetic acid, none. Microscopic examination gave negative results.

*Course.*—Following admission, the child was found to have difficulty in swallowing. Fluids were administered by hypodermoclysis. The condition became progressively worse, and she developed almost constant, twitching, myoclonic convulsions, involving the right arm particularly. The temperature rose steadily during the night.

April 30: The patient was moribund, and the convulsions had ceased. There was marked weakness of the left arm and leg. The patient fumbled with the right hand. Otoscopic examination revealed redness of the right drum; the left drum was normal in appearance. The patient died at 8 p. m., twenty-four hours after admission to the hospital.

*Autopsy* (Dr. J. Werne) (April 11).—There was a bluish discoloration of the dura over the posterior portion of the left parietal lobe, immediately adjacent to the longitudinal sinus, the size of a dollar. When the dura was stripped, this was found to be due to antemortem clotted blood. There was marked injection of the subadjacent tissues of the brain. The subarachnoid space was not encroached on by the hemorrhage. Over the cortical surface of the brain were numerous dotted hemorrhages. The vessels were everywhere engorged. There was no gross exudate. Section showed no evidence of hemorrhage into or dilatation of the ventricles. There were numerous pinpoint hemorrhages and marked congestion in both the gray and the white matter.

The anatomic diagnosis was: (1) acute encephalitis (after measles); (2) limited left subdural hemorrhage. The cause of death was acute encephalitis.

*Histologic Study.*—The meninges showed the same type of congestion as that reported in case I. Here also there was a certain amount of diapedesis with here and there small hemorrhages. The brain substance was also the seat of a diffuse congestion in which small red thrombi occurred here and there. The intensity of the pathologic process was not as marked as in case I. In the cortex there was a distinct disturbance of the lamination in the frontoparietal areas due to considerable proliferation of cellular elements, either free or surrounding the blood vessels. The predominance of the lesions in the frontoparietal cortex might account for the convulsive manifestations in life. In other areas the lesions were much less pronounced, and the various areas of the cortex could be easily detected in most regions. The lesions consisted as usual of the already mentioned cellular proliferation, which was either scattered free in the cortex or surrounding the blood vessels. Some serial sections were made of the frontal area, and we found that the proliferated cells always followed a blood vessel, going through an area apparently free from proliferation. We found, most of the time, that either above or below the proliferated area a blood vessel was detected. Confluence of various

areas of proliferation was also found, especially in the most internal layers. At the boundary between the white and the gray matter, here and there the process was distinctly more pronounced, as in the previous case.

In the white matter the lesions were the more intense and the more diffuse, giving to the white matter the characteristic appearance that has been described in the previous case. The areas of proliferation were numerous and had the same microscopic appearance, the cells being more or less irregular in shape, with irregular nuclei and surrounded by a varying amount of cytoplasm. At times a large mass of proliferated elements was seen surrounding several collected blood vessels.

With appropriate staining, the cellular proliferation appeared to be formed mainly by microglial elements, which had all forms and shapes, varying from the elongated one to the more rounded and occasionally to the typical reticular cells. Astrocytes were also seen in the perivascular areas of disintegration, but their processes appeared fragmented, the whole cell assuming the aspect of the swollen elements undergoing clasmotodendrosis. Far from the most severe areas of disintegration, the astrocytes showed mostly progressive changes, the cells being hypertrophic with long and thick processes.

The nerve cells showed the type of lesion described in case 1, ranging from acute swelling to a severe type of degeneration. Here and there, as in the previous case, elements were seen in a condition of marked ischemia.

The blood vessels showed thicker walls, especially with the Perdrau stain (fig. 9). No spreading of the connective tissue into the surrounding areas, however, was seen, as is found in a true inflammatory process. The specific stain for connective tissue showed in addition that the proliferative elements of which mention is so often made are located mostly outside the vascular sheaths or the mesenchymal network. Some of the small vessels of the cortex disclosed some endarteritic changes consisting of hyperplasia of the lining endothelium.

The nerve fibers showed the same general lesions: demyelination surrounding the blood vessels and forming the characteristic perivascular demyelinated areas. The "U" fibers at the boundary between the white and the gray matter were also lightly involved, the myelin sheaths staining much lighter and some of them even disintegrating. The axis cylinders showed definite signs of disintegration in the same perivascular areas. With appropriate stains we found fat material in the perivascular areas of proliferation only occasionally. Here and there, one or two cellular elements contained such material. At times, fat droplets were encountered free in the tissue. Contrasting with the scarcity of fat in the demyelinated area we found much more of this material in the perivascular spaces free from demyelination. Here elements of various sizes were seen with fat droplets embedded in the cells or free around them.

The pathologic process was diffused through the various cortical and sub-cortical areas, the basal ganglia, the mesencephalon, the pons and the medulla oblongata. In the last two formations the character of its diffusion was analogous to that described in case 1. The wall of the lateral ventricles and the floor of the fourth were the seat of a particular cellular proliferation. The spinal cord was not available for study.

*CASE 3.—Clinical History.*—E. S., a boy, aged 8 years, who was admitted to the hospital on May 5, 1930, had had no previous illness. The present illness began two weeks prior to admission with symptoms and a rash diagnosed as measles by the family physician. On the tenth day of illness, the child became drowsy, slept a great deal and gradually lapsed into coma.

*Physical Examination.*—The patient was in a state of coma. The temperature was 107.6 F.; the pulse rate, 136, and the respiratory rate, 24. He could be aroused slightly by painful stimulation. There was a fine branny desquamation over the entire body with areas of congestion over the bony prominences of the back. The pupils were dilated and equal in size and responded sluggishly to light. There was no nystagmus or strabismus. The ears were normal. There was no nasal discharge or obstruction. The tongue was coated. There was a moderate cervical glandular enlargement. In the lungs, the sounds were clear on auscultation and percussion. The heart sounds were clear; the rate was accelerated, and

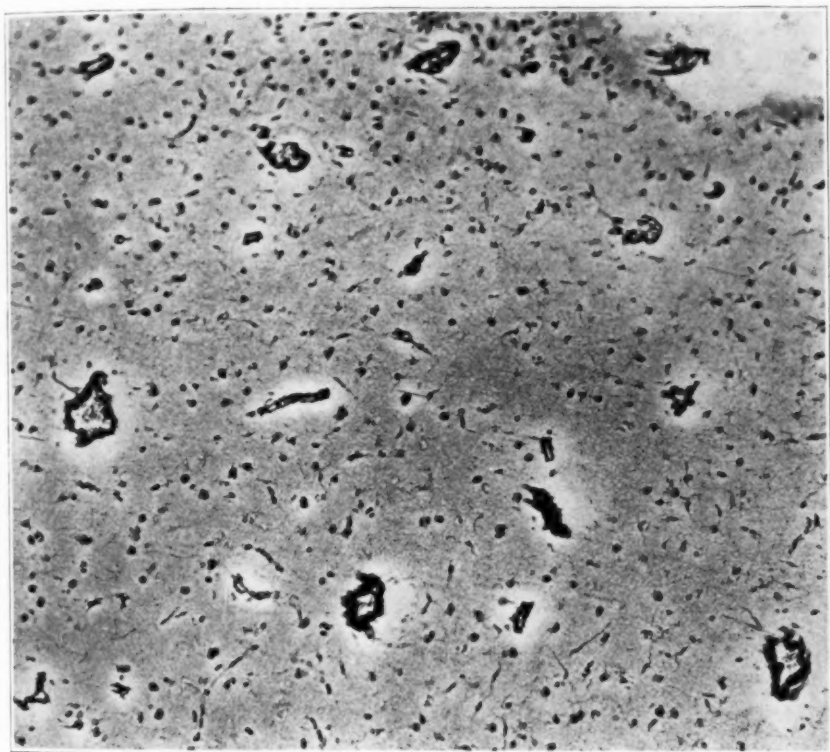


Fig. 9.—Thickening of the walls of the blood vessels, as evidenced by the connective tissue stain. Perdrau's method.

there were no murmurs. The bladder was distended to the level of the umbilicus. There was no nuchal rigidity; the limbs were flaccid. There was a bilaterally positive Kernig sign; the Brudzinski sign was absent; a bilateral Babinski sign was obtained. The knee reflexes were abolished, as were the abdominal and cremasteric reflexes.

*Diagnosis.*—The diagnosis was encephalomyelitis in measles.

*Laboratory Data.*—Lumbar puncture, on admission, revealed clear cerebrospinal fluid under increased pressure; 8 cells per cubic millimeter, all mononuclears; albumin, +; globulin, +; dextrose, +++; no organisms on direct smear; cultures were negative. Urinalysis of a specimen obtained by catheterization on

admission showed that it was clear and of amber color; other observations were: reaction, acid; specific gravity, 1.030; albumin, ++; sugar, acetone and diacetic acid, none. Microscopically, a few epithelial cells, white blood cells and casts were seen. A blood count showed: white cells, 30,280 per cubic millimeter; polymorphonuclears, 90 per cent; lymphocytes, 9 per cent; hemoglobin, 85 per cent.

*Course.*—The condition became rapidly worse. Respirations were labored and at times of the Cheyne-Stokes character. The pulse, though rapid, was of comparatively fair quality. Signs of pulmonary congestion developed. Eight hours after admission, the pulse began to fail; it became weak and thready, and the child became cyanotic. Death occurred a few minutes later.

*Histologic Study.*—The meninges were slightly thickened and considerably congested, with here and there punctiform hemorrhages. Occasionally there was infiltration of blood into the subjacent cortex. The latter was markedly congested, but to a less extent than the white substance. There, also, the blood was in the perivascular sheaths and occasionally infiltrated the surrounding tissues. As in the previous cases, the main histologic characteristic of the process was represented by the presence of diffuse proliferated elements which generally surrounded the blood vessels and especially the veins of both the cortex and the white substance. The proliferated cells gave the impression of a perivascular infiltration, but as a rule no hematogenous elements were seen among them. It must be said, however, that in contrast with the two previous cases, here and there in the cortical white matter and in some of the central formations of the brain, small deposits of lymphocytes were seen and occasionally one or two plasma cells. Most of the proliferated elements were represented by microglia cells which had the same characteristics as have been described in the previous cases. Some of the elements were considerably hypertrophic; others were undergoing acute degenerative changes, while a few of them were transforming into compound granular corpuscles. With scharlach R or Fett ponceau, practically no fat substance was revealed in the areas of demyelination, while here and there, where the last process was less pronounced, fat droplets were encountered either free or embedded in cellular elements.

The astrocytes showed no variations from the reaction already described in the previous cases. In addition, the oligodendroglia cells that stained satisfactorily appeared more or less swollen, while others were atrophic, with shrunken nuclei and deformed cytoplasm.

The myelin sheaths were most severely involved in the perivascular areas where the characteristic areas of demyelination were produced. The axis cylinders showed no changes different from those reported in the previous cases. Here, also, the blood vessels showed somewhat thicker walls, swelling of the endothelium and occasionally an incipient endarteritic process.

In the cortex the proliferated elements were not so numerous as to disturb greatly the cellular architecture. The nerve cells were much better preserved in the outer than in the inner layers, where the pathologic reaction was more pronounced, the involvement of the nerve cells being proportionate to the proliferation. In fact, in the most severe areas of proliferation nerve cells were seen undergoing degenerative changes of varying intensity and character.

The process was more pronounced over the frontal and parietal areas. In the basal ganglia there was a pronounced reaction involving both the lenticular nucleus and the thalamus, and spreading intensely into the internal capsule. The involvement of the mesencephalon was more limited, and the reaction consisted in a slight perivascular proliferation involving mainly the substantia nigra. In the pons the process involved both white and gray matter. In the cerebellum the

white matter alone was affected, the cortex being free from lesions. Surrounding the dentate nucleus the lesions were more severe. In the medulla oblongata the process of proliferation and demyelination was more pronounced at the periphery and all along the floor of the fourth ventricle.

*CASE 4.—Clinical History.*—R. H., a white boy, aged 9 years, who was admitted to the hospital on June 16, 1930, had had diphtheria, varicella, pertussis and, more recently, mumps. The present illness began six days prior to admission with symptoms and a rash diagnosed as measles. On the day prior to admission, the child became drowsy and lethargic, gradually lapsing into a state of coma. There was no vomiting or convulsions.

*Physical Examination.*—The patient was well developed and well nourished, and in a comatose condition. The temperature was 100.6 F.; the pulse rate, 100, and the respiratory rate, 18. There was a fading macular rash on the face and body presenting the appearance of a fading measles rash. The pupils were dilated and equal in size, and reacted to light. The ears were normal. There was no nasal discharge. The tongue was coated; fading Koplik spots were present on the buccal mucosa; the pharynx was injected; the tonsils were enlarged and reddened. There was a slight cervical glandular enlargement. In the lungs, the sounds were clear on percussion and auscultation. The heart sounds were clear; the rate was accelerated, and there were no murmurs. The abdomen was soft, and there were no palpable masses. There was a generalized muscular rigidity and stiffness of the neck. Bilateral Kernig and Babinski signs were present. The knee reflexes were hyperactive; the cremasteric reflexes were present, but the abdominal reflexes were not elicited. There was marked trismus of the muscles of the jaws.

*Diagnosis.*—The diagnosis was encephalitis in measles.

*Laboratory Data.*—Lumbar puncture on admission revealed clear cerebrospinal fluid under markedly increased pressure, containing 44 cells per cubic millimeter, all mononuclears; albumin, +; globulin, +; dextrose, +++; no organisms on direct smear; cultures, negative.

*Course.*—June 17: The patient had two generalized, myoclonic convulsions during the night. The coma persisted. The upper extremities were spastic. The knee reflexes were hyperactive. There was a positive bilateral Kernig sign. The Babinski sign was positive on the left and suggestive on the right side. There was no ankle clonus. The biceps, triceps and radial periosteal reflexes were active. The abdominal and cremasteric reflexes were not elicited. Ophthalmoscopic examination revealed slight blurring of the margins of the disks of both eyes and engorgement of the retinal vessels. Otoscopic examination showed a moderate injection of the periphery of the drum of the right ear; that of the left ear was normal in appearance. There was incontinence of urine and feces. The urine was amber and acid; there was no albumin, sugar, acetone or diacetic acid. The white blood cells numbered 10,700, of which 82 per cent were polymorphonuclears and 18 per cent lymphocytes.

June 18: During the late afternoon and evening, the temperature, pulse rate and respiratory rate began to mount steadily. The child appeared flushed; the skin was warm and moist, and there was an occasional cough. Trismus was marked; mucus collected in the pharynx.

June 19: The patient's condition was poor; the temperature was 104 F., and the respiratory rate, 40 per minute. The pulse was rapid, weak and irregular. The patient was unable to swallow, and mucus collected in the pharynx and oozed out of the mouth.

June 20: The respirations were rapid and labored. Physical examination revealed pneumonia of both lungs. The patient was unable to swallow. Feeding by nasal gavage and administration of fluids by hypodermoclysis were instituted.

June 21: The respirations were labored, with a definite expiratory grunt. The color was cyanotic; the pulse was almost imperceptible. There were coarse tremors of the upper extremities.

June 22: The child died at 12:50 a. m.

*Histologic Study.*—The case was typical of encephalitis in measles in which both the cortex and the white substance were involved by the characteristic lesions already described in the previous cases. The process, however, was more intense in this case and involved diffusely the cortex, the cyto-architecture of which was often disturbed by the considerable accumulation of proliferated elements. There was an evident destruction of nerve cells, which led here and there to the formation of acellular areas. As in the previous descriptions, the perivascular proliferation was formed by the same type of elements, that is, mainly microglia. Often, the proliferated elements appeared to be independent of a blood vessel, but often the relation to a blood vessel could be established.

In the white substance, perivascular proliferation was marked, and areas were found in which the whole field was invaded by proliferated microglial elements. Sometimes there was a continuity between perivascular proliferation involving a group of closely located blood vessels. This is shown in figure 10, in which the microglial elements are collected in large areas, mostly surrounding a few blood vessels.

In the basal ganglia, especially in the caudate nucleus, there was a considerable amount of perivascular proliferation. Underneath the ependyma the proliferated cells were numerous. In the diencephalon and mesencephalon the intensity of the process did not vary from the cortical areas. The cerebellum was slightly involved.

In the medulla oblongata, proliferation was pronounced along the floor of the fourth ventricle. There was besides a diffuse proliferation of elements that were scattered throughout the section and were numerous in the vicinity of the nucleus of the fifth nerve.

The lesions of the myelin sheaths in the perivascular areas, the involvement of the axis cylinders, the neuroglial reaction and the vascular changes, mainly the presence of red thrombi, of thickened walls and of endarteritic changes, were identical with those described in the previous cases. Fat also was present, mostly in the perivascular areas where no demyelination was found.

The spinal cord was not available for microscopic study.

*CASE 5.—Clinical History.*—H. S., a boy, aged 6 years, who was admitted to the hospital on May 6, 1928, had had no previous communicable disease. Appendectomy had been done at the age of 2½ years. Recently he had been exposed to measles at school. The present illness began on April 28, 1928, with loss of appetite. In the evening he was feverish and restless; a cough developed, and he vomited once. During the two following days he was fairly well. On May 1, he appeared sick; he was drowsy, listless, coughed frequently and had no appetite. On the following day, a faint rash appeared on the face. A diagnosis of measles was made by the family physician. Except for the spread of the rash over the body, the child's condition during the two following days was satisfactory. On May 5, he again became acutely ill; he appeared drowsy and feverish, and complained of headache. At this time the rash had begun to fade. During the morning of May 6, the child became comatose; he coughed a great deal, but had no convulsions.

*Physical Examination.*—The patient was undernourished and in a moribund condition; the temperature was 105.6 F.; the pulse rate, 160, and the respiratory rate, 48. There was a generalized, macular mottling of the skin. The gaze was fixed, with conjugate deviation to the right; the pupils were small and equal, and did not react to light. The ears were normal. The mouth was firmly closed; definite trismus was present. The lips were dry and excoriated; sordes was present on the teeth and gums. The tongue was heavily coated; the tonsils were large and reddened; the pharynx was injected, and there was much mucus in the

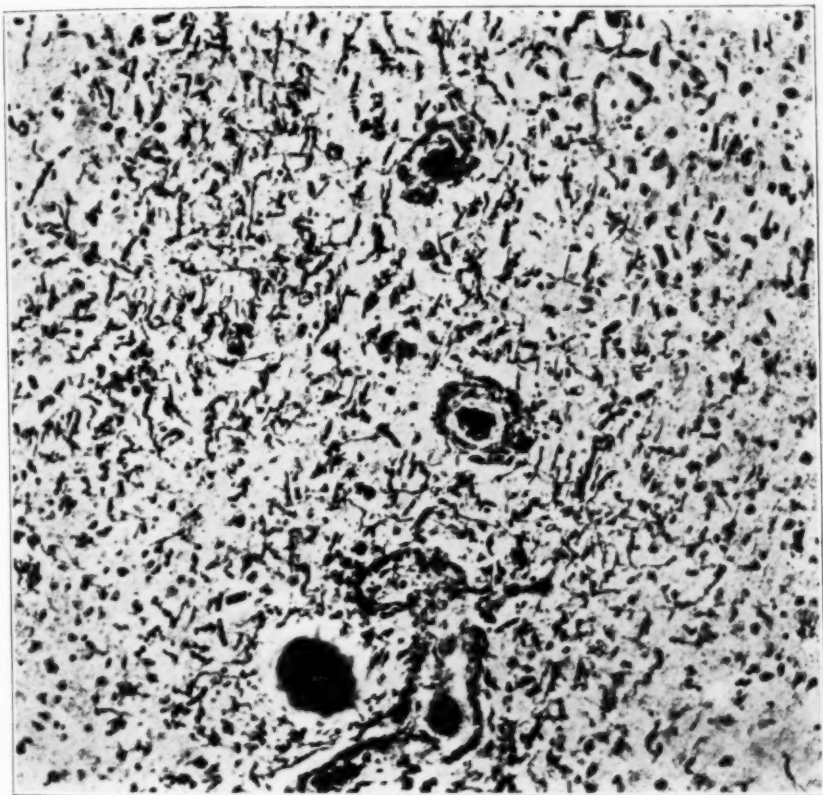


Fig. 10.—Severe involvement of the tissue by proliferated elements of microglial nature. Hortega silver carbonate method (Globus-Penfield modification).

posterior pharyngeal space. The posterior cervical glands were palpable. Coarse râles were heard throughout both lungs. The breath sounds were distant at the inner border of the right scapula and at the left base, and there was impairment of resonance to percussion over the left base posteriorly. The abdomen was soft; the spleen and liver were not palpable. A right rectus scar was present. The external genitalia were normal. There was a slight rigidity of the neck and back; the Kernig and Brudzinski signs were not present; there was no spasticity of the extremities. The knee reflexes and abdominal reflexes were absent. There was a bilaterally positive Babinski sign; no ankle or patellar clonus was elicited.

*Diagnosis.*—The diagnosis was encephalomyelitis in measles and bronchopneumonia.

*Laboratory Data.*—Lumbar puncture revealed blood-tinged cerebrospinal fluid under normal pressure; 8 cc. was removed. No cell count was made on account of the presence of blood; no organisms were found on direct smear. A culture was contaminated. The blood in the cerebrospinal fluid was thought to be due to trauma.

*Course.*—May 7: Coma persisted. The respirations were shallow and rapid. The child's color was poor. The eyelids were closed; there was a slight purulent conjunctivitis; the pupils were equal in size and reacted sluggishly to light. The ears were normal. There was marked trismus of the muscles of the jaws. There was impaired resonance to percussion over the lower lobe of the left lung; the breath sounds over this region were harsh, with many fine and medium coarse râles. The heart sounds were rapid and regular; no murmurs were present. The abdomen was scaphoid. There was no nuchal rigidity and no Kernig sign. The knee reflexes were absent, and there were a bilateral Babinski sign and a bilateral ankle clonus. The abdominal reflexes were absent. The temperature was 106.4 F.; the pulse rate, 168, and the respiratory rate, 60, at 4 a. m. The white blood cells numbered 14,200, with 85 per cent polymorphonuclears, 13 per cent lymphocytes and 2 per cent large mononuclears. At 6 p. m., a blood transfusion of 400 cc. was given. The father, who gave a history of having had measles in childhood, served as the donor.

May 8: The patient's condition was unchanged. Coma persisted. Following the transfusion of blood the child's color improved and the temperature fell to 101 F. with a pulse rate of 152 and a respiratory rate of 60 per minute. By cisternal puncture, clear cerebrospinal fluid was obtained under normal pressure; the cell count was 15 per cubic millimeter, all mononuclears; no organism were seen on direct smear; cultures were negative; albumin was +1; globulin, +1; dextrose, +++.

May 9: The condition was worse. Respirations were labored. The temperature was 105 F., the pulse rate, 160, and the respiratory rate, 60. The child was still comatose. At 5 p. m., a second blood transfusion of 300 cc. was given, this time without any apparent benefit.

May 10: The child died at 1:15 a. m.

*Autopsy* (May 10, at 3 p. m.) (Dr. P. Kreider).—The anatomic diagnosis was encephalitis and myelitis with marked congestion of the blood vessels of the brain and spinal cord and scattered pinpoint hemorrhages in the white matter of the brain and an area of softening, measuring about 1 cm. across, of the white matter of the frontal and parietal lobe; both areas were centrally located not far from the basal ganglia (these two areas histologically were not areas of softening, but areas in which the perivascular proliferation was very pronounced).

*Histologic Study.*—The meninges were the seat of diffuse small hemorrhages. The blood vessels, especially the veins, were engorged. No inflammatory elements were seen. In the cortex there was a severe congestion which at times was more pronounced than the congestion in the white matter. In the white matter small red thrombi were noticeable.

The cyto-architecture of the cortex was grossly well preserved, but more or less disturbance was noticeable in areas in which there was proliferation of nerve elements. This proliferation was mostly evident surrounding the blood vessels, especially the veins. It consisted of cellular elements, some of which had a spindle-

shaped appearance and others a more rounded structure with more or less distorted nuclei. The same proliferated elements were seen free here and there between the various cortical layers.

In the white matter there was a considerable amount of proliferated elements which were located mainly around the veins. Here and there the confluence of

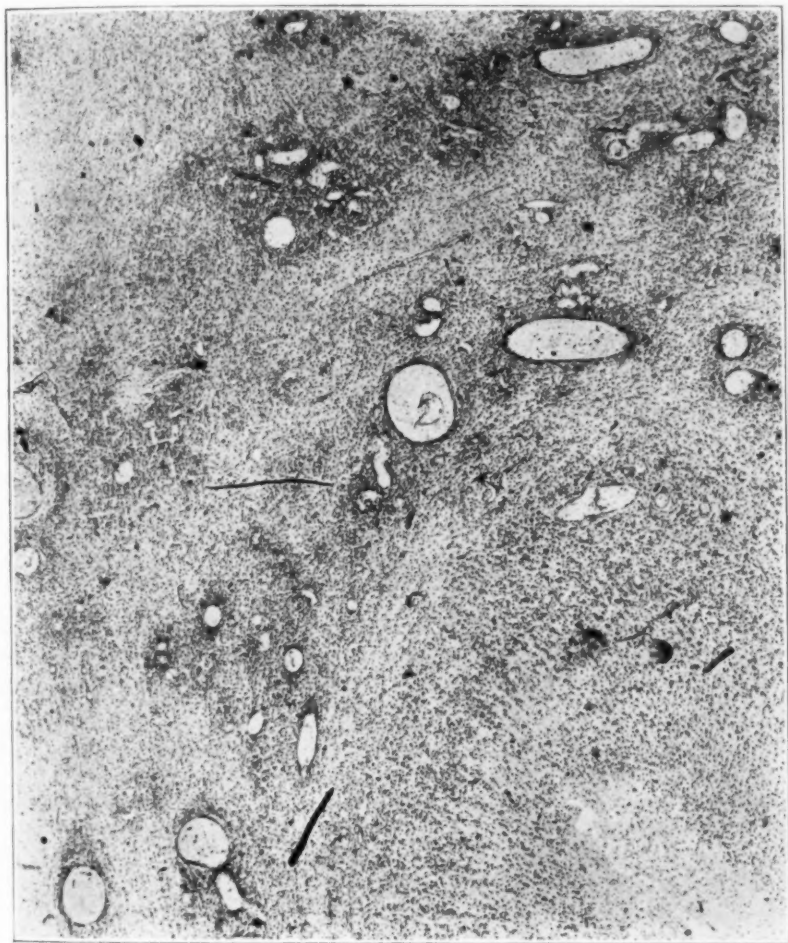


Fig. 11.—Considerable involvement of the white substance by proliferated cells which involve most of the veins, forming a large confluent patch. Nissl stain.

the proliferated elements was such as to invade practically the whole section, as is seen in figure 11.

The perivascular proliferation was diffused in the various cortical areas, mainly the frontal, precentral and postcentral. In the postcentral area, the cyto-architecture was at times poorly recognizable because of peripherally radiating bands in which the tissue was invaded by proliferated elements. At the boundary between

the gray and the white matter, the proliferative changes seemed more pronounced. In the hippocampus the cortical lamination was well preserved, and only a few proliferated elements were encountered. In the pons there was a severe perivascular proliferation which affected both the transverse fibers and the various nuclei; of these, the dorsal nuclei seemed the least affected. In the medulla oblongata there was a diffuse perivascular proliferation which affected severely the area of the trigeminal root. There was also a marginal proliferation involving especially the ventral portion of the medulla (fig. 12). The basal ganglia were the seat of marked perivascular proliferation involving both the white and the gray matter. In the thalamus the medial nucleus seemed mostly affected. The pulvinar was also considerably involved. Of the lenticular nucleus the putamen was much more involved than the globus pallidus. The corpus geniculatum laterale was the seat of severe perivascular proliferation involving especially its lower and internal portions.

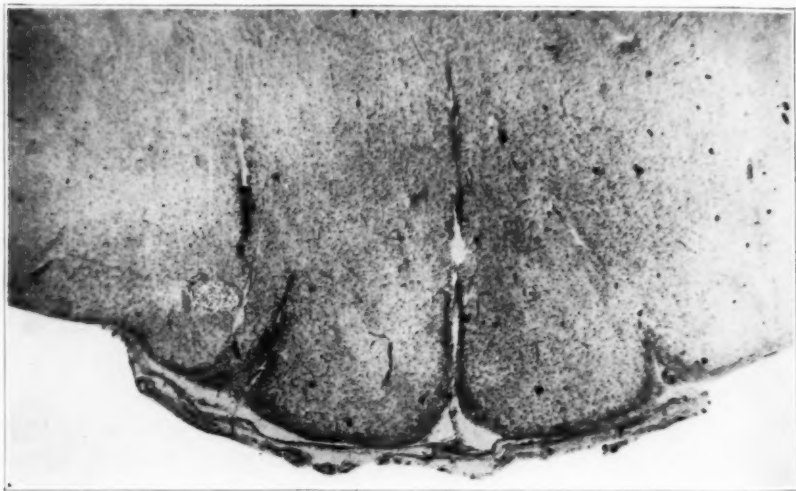


Fig. 12.—Marginal proliferation, especially pronounced along the ventral portion of the medulla oblongata. Nissl stain.

In the cerebellum an occasionally slight perivascular proliferation was found in the lamina molecularis. The white substance was also slightly involved, perivascular proliferation being of a moderate degree and scattered in very small areas. Surrounding the dentate nucleus the lesions seemed more pronounced.

The cells forming the perivascular proliferation were mostly microglial elements undergoing various stages of transformation. Among them some hypertrophic astrocytes were also encountered. The blood vessels of both the cortex and the white substance showed thickened walls, and the small ones of the cortex disclosed some swelling of the endothelium and occasionally hypertrophy and hyperplasia of the same layer leading to an endarteritic process. The perivascular areas were the seat of a process of demyelination in which both myelin sheaths and axis cylinders were disintegrated. In the cervical region of the spinal cord the sulcus spinalis anterior appeared somewhat widened. Marginal proliferation was seen along both anterior and posterior columns. Perivascular proliferation was seen in the anterior columns. In the posterior columns the columns of Goll

were practically free from proliferation, while the columns of Burdach and the zone of entrance of the posterior root disclosed evidences of proliferation. In the thoracic segments, the gray matter was dominantly involved. In the lumbar region, marginal proliferation was again evident and more pronounced at the zone of entrance of the posterior root. Areas of marked demyelination were found in the posterior column, especially in the columns of Goll. The areas involving these columns seemed symmetrical (fig. 13). The details of the histologic process did not vary from those described in the brain.

**CASE 6.—Clinical History.**—M. L., a white girl, aged  $4\frac{1}{2}$  years, who was admitted to the hospital on June 14, 1928, had previously had mumps and pertussis. In May, 1927, she was knocked down by an automobile and was unconscious for several hours; she made an uneventful recovery. In January, 1928, the child had an attack of coryza, sore throat and fever, and subsequently cervical adenitis developed with an accompanying rigidity of the neck and back. She was sick for twenty days; the illness was not accompanied by any exanthematous manifestations; recovery was complete. The present illness began on June 9, when the child became indisposed. She was cranky and feverish and had coryza

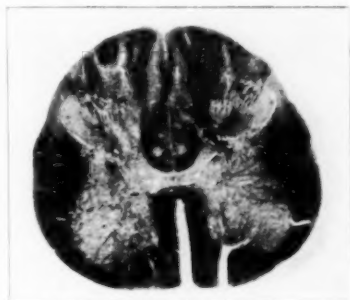


Fig. 13.—Lumbar segment of the spinal cord, showing considerable involvement of the posterior columns. Spielmeier's method for myelin sheaths.

and general malaise. Between June 9 and 13, three other children in the family developed measles. On June 13, the patient awoke with fever and a generalized measles rash. At 11 a. m. the child had paralysis of all the extremities. There had been no prodromal symptoms preceding the paralysis, no vomiting and no convulsions. The child remained conscious. An hour later she vomited. At 3 p. m. she became drowsy. Bilateral strabismus developed and the jaws became fixed. On June 14, the child was in a state of coma.

**Physical Examination.**—The patient was well developed and well nourished and was in a comatose condition. The temperature was 106.2 F., the pulse rate, 178, and the respiratory rate, 60. She could be aroused to restlessness by painful stimulation. Respirations were of the Cheyne-Stokes character. A macular and punctate hemorrhagic rash was present on the face, body and extremities; no recent hemorrhages were present. The picture was that of a hemorrhagic measles rash that was beginning to fade. There was a small amount of dried secretion in the nares. There was no rigidity of the neck; the upper limbs were spastic, the lower limbs flaccid. The knee reflexes and ankle jerks and the abdominal reflexes were absent. There was a bilaterally positive Babinski sign; the Kernig and Brudzinski signs were negative. There was no facial asymmetry. The eyelids

were half open; there was a bilateral internal strabismus; the pupils were unequal in size, the right being smaller than the left; neither reacted to light. There was a purulent conjunctivitis; the corneas and scleras were dull. The drums of both ears were slightly dull, but there was no redness or bulging. The jaws were firmly clenched; the mouth could be opened only with considerable force. The pharynx was injected, and mucus was collected in the posterior pharyngeal space. There was a generalized lymphatic glandular enlargement. There was impairment to percussion over the base of the left lung posteriorly from the angle of the scapula; medium and coarse inspiratory and expiratory râles were heard over both lungs. The heart sounds were clear; the rate was accelerated, and there were no murmurs. The abdomen was normal, except for a distended bladder, which reached the level of the umbilicus.

*Diagnosis.*—The diagnosis was encephalomyelitis in measles; bronchopneumonia.

*Laboratory Data.*—Lumbar puncture on admission revealed clear cerebrospinal fluid under apparently normal pressure; cell count, 48 per cubic millimeter, consisting of 34 mononuclears, 8 polymorphonuclears and 6 red blood cells; albumin, +; globulin, +; dextrose, +++; a direct smear showed no organisms; cultures were negative. A blood count gave hemoglobin, 75 per cent; red cells, 4,700,000; white cells, 11,500, with 78 per cent polymorphonuclears, 18 per cent lymphocytes and 4 per cent large mononuclears. A specimen of urine obtained by catheterization was amber, clear and acid; no albumin or sugar was present. Microscopic examination showed epithelial cells and an occasional pus cell.

*Course.*—June 5: At 1 a. m., blood transfusion was performed, the father serving as donor; 300 cc. of blood was given by the direct syringe method. Following the transfusion the child's condition appeared to be slightly improved; the color was better and the pulse stronger. At 2:45 a. m., the child became very restless, crying out at intervals. At 4 a. m., the respirations became slow and irregular and tracheal râles were audible. The child died at 5 a. m.

*Autopsy* (June 5, 4 p. m.) (Dr. P. Kreider).—The anatomic diagnosis was encephalitis with moderate hyperemia of the vessels of the brain and meninges and pinpoint hemorrhages in the white matter, especially in the region of the corona radiata; hyperemia of the pia mater of the cord; confluent bronchopneumonia in the stage of red hepatization in the posterior portion of the left lower lobe. The cause of death was measles with pneumonia and encephalitis.

*Histologic Study.*—There was marked congestion of the meninges accompanied by a certain amount of diapedesis. Here and there were small hemorrhagic foci which could also be detected in the gray matter. There was no perivascular infiltration.

There was marked hyperemia of the cortex. The lamination was generally well preserved, with the exception of areas in which there was an accumulation of cellular elements generally surrounding one or more blood vessels. At times the proliferation of the cellular elements was more diffuse, and its connection with the blood vessels was less definite. At the border between the white and the gray matter there was often a more considerable accumulation of proliferated elements, generally confined to a territory surrounding blood vessels.

In the white substance the histologic picture was characteristic and was represented by more or less diffuse and numerous foci of cellular elements which were scattered throughout the section and which generally surrounded blood vessels, particularly veins. When the number of foci was considerable, the section might acquire even macroscopically a peculiar appearance in which blood vessels were seen

considerably congested and surrounded by deeply stained areas that might give the impression of areas of softening.

The same changes were found in practically all the cortical areas that were examined; precentral, postcentral, temporal and occipital. There was, however, a variety in the intensity of the lesions, the changes being less pronounced in the temporal and occipital lobes than in other areas.

In the hippocampus the lesions were present with their typical character, while in the basal ganglia both the putamen and the globus pallidus appeared considerably involved. Numerous areas of perivascular proliferation were seen in the internal capsule and in the various nuclei of the thalamus. In the pons the lesions were pronounced and seemed to involve mainly the various nuclei.

In the medulla oblongata the same proliferative changes were diffused all over in the white substance and along the periphery. In the cerebellum the lesions were not very pronounced. They did not involve the cortical layers, but were evident in the white substance. Marked proliferation was noticeable in the subependymal layers of both the lateral and the fourth ventricle.

In the spinal cord there was also a definite marginal proliferation which was apparent not only at the periphery but also along the sulcus medianus anterior and posterior. A few areas of proliferation were seen free in the white substance, being occasionally more pronounced in the gray matter. The marginal proliferation was present at various levels of the cervical, thoracic and lumbar segments. In the lumbar region the lesions seemed more pronounced in the posterior columns.

Wherever the perivascular proliferation was present, the other lesions involving nerve fibers, glia cells, blood vessels and fat products of disintegration were of the same type as those described in the previous cases.

#### COMMENT

From a histopathologic standpoint, the six cases reported show lesions that are practically the same in all. They consist mainly of a perivascular proliferation formed especially by microglial elements. The microglial nature of the cell is brought out beyond doubt by the specific methods of silver impregnation.

In some of the cases there were scattered elements of hematogenous nature in the perivascular areas. These elements were mainly lymphocytes, but occasionally plasma cells. The perivascular hematogenous elements were never of great importance, and in some cases there was no trace of them in all the material studied. The perivascular proliferation was dominantly located in the white substance, where it formed large islands. The cortex, however, was involved by the same process, although to a much less extent.

Accompanying the perivascular proliferation there is a concomitant perivascular demyelination, which forms another characteristic of the pathologic process. Lesions involving the axis cylinders are to be expected in demyelinated areas and have been reported in all our cases. Less characteristic is the macroglial reaction with both its progressive and its regressive changes. A fact that has not been emphasized sufficiently in the reports of other authors is the frequency of thrombi (red

thrombi) and the occurrence of vascular changes, swelling or hyperplasia of the endothelium. Although these manifestations are not dominant, they are undoubtedly present, and their existence may help to explain the pathogenesis of the lesions. They certainly point to a participation of the vascular system in the process, and this fact, associated with the one that most of the lesions are perivascular in topography, justifies the hypothesis that whatever noxious agent is the cause of the lesions this agent is carried from the blood vessels to the surrounding tissue and is favored by an abnormal permeability of the protective wall and stasis of the venous system. A similar view was expressed by Wohlwill, who believed that when the blood stream becomes slow, as in the veins, some substance passes out of the blood vessel and diffuses into the parenchyma; also, through communications between the adventitial and subarachnoid spaces it mixes with the spinal fluid and thus affects the parenchyma bordering on the inner and outer surfaces of the brain and cord.

In the presence of a perivascular reaction, consisting mainly of microglia and without hematogenous elements, are we justified in speaking of an inflammation in our cases? This is a difficult question to answer. If, as Spielmeyer<sup>12</sup> pointed out, by inflammation one understands the occurrence of a perivascular exudate formed by hematogenous elements, that is, lymphocytes and plasma cells, to which a connective tissue reaction could be added, then one should not speak of inflammation in our cases. On the other hand, if the conception of inflammation includes every form and type of general reaction of a tissue to pathologic stimuli, even if the reaction involves elements usually unaffected, one might speak of inflammation. Personally, we believe that in order to avoid confusion one should limit the term inflammation to processes in which the perivascular reaction fits into the classic conception of an exudate of hematogenous origin. If later studies prove that in infectious processes other reactions may occur that are comparable to those typical of encephalitis in measles, we shall gladly change our minds.

The fact remains that in encephalitis in measles there is a characteristic process which has attracted the attention of investigators only recently, the few older reports being incomplete as to the nature of the perivascular elements. Spielmeyer, who undoubtedly has had an unusual experience in neuropathology, wrote that he never before saw such a type of reaction in the central nervous system. Because of the peculiar type of reaction, so different from a typical inflammatory reaction, we are inclined to adopt the term encephalopathy instead of encephalitis.

12. Spielmeyer, W.: Die nichteitrige Encephalitis im Kindesalter, *Monatschr. f. Kinderh.* **44**:195, 1929.

The same type of lesions has been described in vaccine encephalitis (Turnbull and MacIntosh,<sup>13</sup> van Bastiaanse,<sup>14</sup> Perdrau,<sup>15</sup> Hassin and Geiger,<sup>16</sup> Lucksch,<sup>17</sup> Bouman and Bok,<sup>18</sup> Wiersma<sup>19</sup> and others), in influenza (Greenfield<sup>20</sup> and Bassoe and Grinker<sup>21</sup>) and in rabies vaccine (Bassoe and Grinker<sup>22</sup>). In all of these conditions the histologic lesions were comparable to and even identical with those described in encephalomyelitis following measles. There must then be a link between these various pathologic conditions; this brings up a discussion of the etiology of acute encephalomyelitis.

There are at present three main views of the encephalitis that follows vaccinations or acute exanthematous diseases: (1) that the lesions in the brain and cord are due directly to the action of the virus of smallpox, vaccinia or measles (MacIntosh and Turnbull, Lucksch and Gorter and van Nederveen<sup>23</sup>); (2) that they represent an allergic or anaphylactic phenomenon occasioned by the preceding illness (Glanzmann,<sup>24</sup> Rivers<sup>25</sup>

13. Turnbull, H. M., and MacIntosh, J.: Encephalomyelitis Following Vaccination, *Brit. J. Exper. Path.* **7**:181, 1926.

14. van Bastiaanse, B.; Bijl, J., and Terburgh, J.: Encéphalite consécutive à la vaccination antivariolique, *Bull. Acad. de méd., Paris* **94**:815 (July) 1925; Encéphalite postvaccinale, *Nederl. tijdschr. v. geneesk.* **2**:1267 (Sept. 18) 1926.

15. Perdrau, J. R.: The Histology of Postvaccinal Encephalitis, *J. Path. & Bact.* **31**:17, 1928.

16. Hassin, G. B., and Geiger, J. C.: Postvaccinal (Cowpox) Encephalitis: Clinicopathologic Report of Case, *Arch. Neurol. & Psychiat.* **23**:481 (March) 1930.

17. Lucksch, F.: Blatternimpfung und Encephalitis, *Med. Klin.* **20**:1170 (Aug.) 1924; Gibt es beim Menschen eine Vakzine-Encephalitis? *Centralbl. f. Bakteriolog.* **96**:309, 1925.

18. Bouman, L., and Bok, S. C.: Die Histopathologie der Encephalitis post-vaccinationem, *Ztschr. f. d. ges. Neurol. u. Psychiat.* **111**:495, 1927.

19. Wiersma, D.: Encephalitis After Vaccination, *Acta psychiat. et neurol.* **2**:167, 1927.

20. Greenfield, J. G.: Acute Disseminated Encephalomyelitis as a Sequel to Influenza, *J. Path. & Bact.* **33**:453 (April) 1930.

21. Bassoe, Peter, and Grinker, Roy R.: Human Rabies and Rabies Vaccine Encephalomyelitis: Clinicopathologic Study, *Arch. Neurol. & Psychiat.* **23**:1138 (June) 1930.

22. Bassoe, P., and Grinker, Roy R.: Disseminated Encephalomyelitis and Its Relation to Other Infections of the Nervous System, *Tr. Am. Neurol. A.* 1930.

23. Gorter, E., and van Nederveen, H. J.: Ueber unsere Kuhpockenimpfung, *Nederl. tijdschr. v. geneesk.* **2**:1746 (Oct. 22) 1927; **2**:2026 (Nov. 12) 1927; abstr., *Zentralbl. f. d. ges. Hyg.* **17**:63, 1928.

24. Glanzmann, E.: Die nervösen Komplikationen der Varizellen, Variola, und Vakzine, *Schweiz. med. Wehnschr.* **57**:145, 1927.

25. Rivers, T. M.: Viruses, *J. A. M. A.* **92**:1147 (April 6) 1929.

and Keller<sup>26</sup>); (3) that they are caused by an unknown virus or toxin which is in some way empowered by the exanthematous disease to attack the nervous system (Levaditi, Nicolau and Sanchez-Bayarri,<sup>27</sup> Pondman,<sup>28</sup> Keller,<sup>29</sup> Pette,<sup>30</sup> Wohlwill, Greenfield and Hassin).

Against the first view would be the fact that infection of the brain in rabbits or monkeys with vaccinia produces a very different histologic picture from that of postvaccinal encephalitis. The virus tends to attack the meninges primarily and, according to the work of Hurst and Fairbrother,<sup>31</sup> the essential lesion is a "fibrinous hemorrhagic and polymorphonuclear meningitis." There are in addition such alterations as may be present in the underlying nerve structures, and "they are seen only where the meningitis is most severe and are no doubt due, at any rate in part, to disturbances in nutrition consequent upon this and upon compression resulting from the intense local edema." According to the same authors, it is hardly possible to imagine a greater contrast between this picture of vaccinal encephalitis and that seen in disseminated encephalomyelitis following vaccination in which the meninges are normal or only slightly infiltrated in places with mononuclear cells that have probably drained along the perivascular spaces from the deeper tissues.

In contrast with the report just mentioned is one of MacIntosh and Scarff,<sup>32</sup> which appeared in the same number of the *Journal of Pathology and Bacteriology*, claiming that virulent strains of vaccinia can produce in rabbits a definite meningo-encephalitis after intracerebral, intravenous and intradermic inoculation. The lesions produced are directly comparable with the visceral lesions in rabies and with those of postvaccinal and postvariolar encephalitis in man. With contrasting results of this nature the wisest thing to do is to wait for confirmation of either one or the other before deciding in favor of any

26. Keller, W.: Ueber Erkrankungen des Zentralnervensystems im Anschluss an die Kuhpockenimpfung, *Nervenarzt* **1**:729 (Dec.) 1928.

27. Levaditi, C.; Nicolau, S., and Sanchez-Bayarri, V.: L'étiologie de l'encéphalopathie, *Presse méd.* **35**:161 (Feb. 5) 1927.

28. Pondman, A.: Bacteriological Researches in Post-Vaccinal Encephalitis, *Nederl. tijdschr. v. geneesk.* **2**:2037 (Nov. 12) 1927.

29. Keller, quoted by Pette, H.: Das Problem der postvakzinalen Encephalitis: Eine experimentell biologische Studie, *München. med. Wchnschr.* **75**:207 (Feb. 3) 1928.

30. Pette, H.: Die Stellung der postvakzinalen Encephalitis in der Reihe infektiöser Erkrankungen des Zentralnervensystem, *Centralbl. f. Bacteriol.* **110**:134 (Jan.) 1929.

31. Hurst, E. W., and Fairbrother, R. W.: Experimental Vaccinal Encephalitis in the Monkey and the Rabbit, *J. Path. & Bact.* **33**:463 (April) 1930.

32. MacIntosh, J., and Scarff, R. W.: The Reaction of the Central Nervous System to Vaccinia Virus, *J. Path. & Bact.* **33**:483 (April) 1930.

difference between natural and experimental encephalitis. Nevertheless, the negative results of Hurst and Fairbrother do not allow one to accept, for the present at least, the first hypothesis in discussion.

The hypothesis of an anaphylactic phenomenon is, according to Greenfield, supported by the case of a transitory paraplegia following antirabic treatment, and by a fatal case of this kind in which Babes and Mironesco<sup>33</sup> found a condition closely resembling acute disseminated myelitis. If the condition were due to an anaphylactic response, however, one would have expected that it would have been discovered in some of the fatal cases of tetanus or diphtheria following the injection of an antitoxic serum. It is conceivable that some kind of reaction occurs in virus infections which might loosely be called anaphylactic, but which is different from an anaphylactic reaction due to a foreign protein.

The third hypothesis, that the condition is caused by an unknown virus or toxin, is equally problematic, but is to some extent supported by instances of cases of encephalitis or myelitis following vaccination, smallpox, measles, rabies and influenza. According to Greenfield, there is no doubt that all these forms have occurred much more frequently during the last few years than at any period since the beginning of the present century, but the pathologic records of Westphal and Barlow and Penrose indicate that this is not a new disease; on the clinical side, similar nervous complications were known after smallpox a century ago and after measles two centuries ago. While an alteration in the virulence of the virus of vaccinia so that it acquires a special virulence for the nervous system is conceivable, it is highly improbable that a similar alteration would during certain years affect also the virus of measles and that of influenza. Bassoe and Grinker, who minimized the ability of the neuropathologist to determine the toxic, bacterial or virus origin of any disease, considered it possible that a whole group of different viruses may be responsible and must be sought in all types of encephalitis without reference to their pathology.

In the present state of knowledge it seems to us that acute disseminated encephalomyelitis is most likely a toxic reaction of the central nervous system occurring in a number of different virus infections. In favor of this conception one must consider a particular type of lesion of the nerve cells that may be definitely related to exogenous intoxications of chemical nature. By this we mean the acute type of lesion of Nissl, the so-called liquefaction (*Verflüssigung*) of German authors. In our collection of cases of encephalomyelitis following measles we have two cases that will form the subject of a separate description; in

33. Babes, V., and Mironesco, C.: La paralysie ascendante mortelle survenue après le traitement anti-rabique. *Compt. rend. Soc. de biol.* **64**:965, 1908.

the two of them, although inflammatory changes and even the characteristic perivascular proliferation are absent, there is a diffuse cortical involvement consisting mainly in the liquefaction of most of the nerve cells. The lesions compare exactly with the ones seen in other exogenous toxic conditions, as for instance lead poisoning, and thus favor greatly the hypothesis which we favor of a toxic origin of the lesions.

Dr. J. Neal supplied the brain material in cases 1, 2, 3 and 4. Dr. P. Kreider, formerly pathologist of the Willard Parker Hospital, permitted us to use the pathologic material in cases 5 and 6, which will form the subject of a detailed study of his own. Dr. J. Werne, pathologist at Queensboro Hospital, permitted us to use his general postmortem observations in case 4.

ABSTRACT OF DISCUSSION ON PAPERS BY DRS. GRINKER AND BASSOE AND  
DRS. FERRARO AND SCHEFFER

DR. GEORGE B. HASSIN, Chicago: It is rather hard to discuss in a few minutes the subject covered by Dr. Grinker and Dr. Bassoe in their presentation. They even failed to give a definition of disseminated encephalomyelitis, or to tell what they meant by this morbid condition. The cases recorded by them show a great variety of clinical and pathologic manifestations. One must thus assume that disseminated encephalomyelitis cannot possess a specific or a definite clinical picture, as the lesions are scattered throughout the central nervous system, varying in their extent, localization and structure. From the presentation I gather that it is not possible, from the pathologic data, to form conclusions concerning the nature of a disease process, whether it is inflammatory or degenerative. Dr. Grinker's conclusion is that the foci, as seen in multiple sclerosis, in Heine-Medin's disease, in epidemic encephalitis and in similar conditions, signify an acute nonsuppurative encephalitis. This is hardly so. In Heine-Medin's disease, for instance, the foci are represented mainly by perivascular hematogenous infiltrations—lymphocytes, plasma cells and polyblasts. Such so-called infiltrative phenomena are also seen in epidemic encephalitis, typhus fever, dementia paralytica and many other conditions caused by an infection. Often such perivascular infiltrations are combined with nodules that consist mainly of glia cells. It is a strong temptation to look on these infiltrations and nodules as signs of a parasitic invasion. Such a view is supported by what one sees in encephalitis caused by an infection with *Trichinella* in which both the lymphocytic and glial infiltrations harbor embryos of *Trichinella*. Dr. Grinker seems to consider the lymphocytic infiltrations of minor importance.

Another group of cases, the foci of which grossly resemble those of the previous group, consists mainly, if not exclusively, of fat granule bodies (gitter cells). This is seen in multiple sclerosis, subacute combined degeneration of the cord, amyotrophic lateral sclerosis, Schilder's disease and many other degenerative states. Lymphocytes or plasma cells may be seen, but only occasionally. As a rule, they are absent, just as gitter cells are generally absent in perivascular lymphocytic infiltrations. The probable cause of the foregoing lesions is not an infection, but an intoxication.

In the third group of cases both inflammatory and degenerative phenomena may be equally represented. This occurs with remarkable constancy in the cases which Dr. Bassoe and I described as multiple degenerative softening, but which proved to be, from Diamond's studies, cases of severe toxemia or septicemia. Here I would include Dr. Grinker and Dr. Bassoe's case 3. Such cases have a

subacute course (of weeks or several months), show a combination of degenerative and infiltrative phenomena and are often referred to as acute multiple sclerosis. In contrast to such subacute cases, conditions occur in which degenerative foci occur within a few days, as, for instance, in postvaccinal encephalitis.

The few instances show that histologic changes of disseminated foci vary according to the etiology, age and extent of the reactive, mesodermal and ectodermal phenomena shown by them. To do justice to these factors a large variety of cases must be studied and the observations contrasted before the statement made by Dr. Grinker, that there is "no adequate reason for considering such diseases as multiple sclerosis, Schilder's disease, as primarily degenerative," can be considered.

DR. WILLIAM G. SPILLER, Philadelphia: In a paper on this subject that I reported before this Association last year, I included a number of cases of different types under the name of disseminated encephalomyelitis. I shall refer briefly to a case of multiple sclerosis included in that paper. It was particularly interesting, as the lesions in the spinal cord were evidently of much longer duration than those in the brain. The lesions in the spinal cord looked very much like the areas of multiple sclerosis that we commonly find in this disease, but all through the parts of the brain that I examined there were areas of microglia cells (gitter cells), and the lesions were of much more recent development than the lesions in the spinal cord, so that the process in this acute multiple sclerosis, which is a disease probably more common than we have been inclined to think, is one which is not of the same intensity in all parts of the central nervous system at the same time.

DR. SIMON P. KRAMER, Cincinnati: I think that there is no more important neurologic problem today than the study of encephalitis. I have been doing some work in postvaccinal encephalitis. We have at the laboratory a strain of vaccine virus with which we have no difficulty in producing encephalitis in 100 per cent of experiments, with intracerebral inoculation into rabbits. This vaccine also readily passes the Berkefeld filter, but I have never been able to produce encephalitis with the Berkefeld filtrate of this virus, although it gives a "take" on the skin.

While I am not yet sure or at all dogmatic about it, I feel that in postvaccinal encephalitis we may be dealing with a picked-up virus.

I have also thought about the cases that Dr. Kennedy reported, which he ascribed to angioneurotic edema following the injection of autotoxic serums. I think that in these cases we must also think of the possibility of a picked-up virus.

Our antitoxic serums are the serums of horses, Berkefeld filtered, plus 0.5 per cent of phenol. If you subjected vaccine virus to these procedures, you would still have living virus. You would not necessarily disinfect a serum from a virus similar to a vaccine virus or to a rabies virus.

I have listened tonight to a great deal of morphology. Morphology is an excellent thing, but it is not an end in itself, and I have heard no young men say that they have put any of this material into the brain of a monkey; but yet, naturally, if I were investigating a virus, a first cousin, let us say, to a poliomyelitis virus, that would be the only way in which I could demonstrate it. I would be able to demonstrate only a hypothetical virus similar to poliomyelitis virus by that method.

I would also like to bring up the cases of so-called Jamaica ginger paralysis. Some of you may have seen some of these so-called "jake" paralyzes, paralyzes that have been ascribed to the ingestion of Jamaica ginger. There are possibly 50,000 people in the United States who have this disease. We have hospitalized more

than 300 patients in Cincinnati, and there are probably 1,000 cases. I went to a village near Cincinnati, with a population of 1,200, where there were 100 cases, and one physician had 64. I am not convinced that these cases are due to poison. There is a possibility of their being infectious. The clinical history in these cases is that they begin with a foot drop and then a wrist drop. They do not clear up. They have been diagnosed as peripheral polyneuritis. The autopsy material (there has been some autopsy material) shows no changes in the peripheral nerves, but does show marked destruction of the anterior horn cells in the cervical and lumbar regions of the spinal cord. There is no sign of an inflammatory reaction. There is not the inflammatory reaction of poliomyelitis, but there is distinct degeneration of the anterior horn cells. I know of no chemical poison that would do this; nor has there been found in the preparations of ginger examined any poison capable of producing a lesion of the anterior horn cells. I do, however, know of an infection virus that does cause these cellular changes.

DR. ADOLF MEYER, Baltimore: Being one of those who for a long time had to work largely on autopsy material that was borrowed, I should like to emphasize a point that is brought home by Dr. Kramer's remarks, namely, the tremendous importance of being prepared in cases of autopsy to do biologic as well as morphologic work. It seems to me that that sort of thing has hardly received enough attention because some of us are only one-sidedly trained, and when we obtain the brain for study, we are left more or less at sea for lack of data, especially on biologic problems.

The work that Dr. Hassin has done goes a long way toward getting us keyed up from the point of view of chemistry. What Dr. Cobb has shown demonstrates the equivalent of earthquakes occurring in the nervous system, and I think that we have to add other biologic methods as well and perhaps bring about a reform in this respect—autopsies on nervous material should be done by physicians who know the nervous system and also the various things likely to involve the nervous system through the physiologic and biologic condition of the other organs and functions.

DR. LAWRENCE S. KUBIE, New York: There is one point that seems to me to make it difficult to distinguish inflammatory from degenerative processes. To begin with, there is the debated question of whether lymphocytic infiltration is hematogenous or local in origin. There is evidence that points to the fact that the perivascular tissue is lymphoblastic, and that even in normal animals there is constantly a formation of lymphocytes occurring along the perivascular apparatus. If this is so, the stimulation of this lymphoblastic tissue to an increased rate of formation of lymphocytes is necessarily a slow process which will depend on the nature and intensity of the stimulus at any one point. Therefore, as Dr. Hassin said, the time element must be important. There is more than a time element, however, because along any vessel one may see at one point an intense lymphocytic infiltration and a little further along the same vessel an accumulation of macrophages. I have found this in experimental work; and I was interested to learn that Dr. Greenfield has made the same observation in human material.

Obviously, then, the nature of the cellular reaction that occurs in a person or in an experimental animal is going to depend on certain local factors. The type of cellular reaction, therefore, will rarely justify one in classifying the entire picture as inflammatory or degenerative.

Furthermore, in arguing from the presence or the absence of perivascular infiltrations of lymphocytes, one must keep in mind the fact that these lymphocytes are extraordinarily mobile, and that they can be mobilized by factors of pressure

and drainage. That has been proved, I believe, in the experimental use of forced drainage. At the National Hospital, Queen Square, London, I have had the opportunity to examine, with this point in view, a group of perhaps a dozen cases of poliomyelitis and of epidemic encephalitis. These cases had interested Dr. Greenfield because certain of them had very intense symptoms but extraordinarily little perivascular infiltration. I think that any one who has seen a great deal of material from cases of poliomyelitis and encephalitis has encountered occasional severe cases in which the absence of infiltration has been surprising. From the hospital records of these cases it was possible to correlate the amount of infiltration with the number of lumbar punctures that had been performed for diagnostic purposes. We found, as we had suspected, that with one exception the more frequent and more recent the lumbar punctures, the less severe was the perivascular infiltration. Therefore, a factor of mechanical drainage must also be kept in mind before one concludes from the absence of infiltration that a process is degenerative rather than inflammatory.

DR. ROY R. GRINKER, Chicago: It is interesting that we had an opportunity to compare encephalitis following measles, as shown by Dr. Ferraro, with that following an infection of the upper respiratory tract, and one can see that the pathologic picture is practically the same. I must confess that I do not understand the word "toxic." Toxic to what? We are justified in using the term toxic etiologically in the presence of some known exogenous agent such as lead, arsenic or alcohol or in the presence of some definite, regularly demonstrable, endogenous source such as a distant infection or tissue destruction. To use the term toxic as an explanation of these doubtful infections or degenerative diseases is but to beg the question.

Dr. Hassin brought up some interesting problems. It is true that there is one large group of encephalitis, rabies, epidemic encephalitis, poliomyelitis and Bornu's disease in which there is a tremendous perivascular lymphocytic infiltration that usually diffuses into the brain tissue itself. One can hardly differentiate these diseases from each other except by knowing the location of the greatest change. But the perivascular infiltration of lymphocytes may be found equally intense when there is absolutely no infection and when the inflammation is secondary to a destruction of tissue, and one can hardly differentiate as massive an infiltration that occurs in the perivascular spaces in these cases from the encephalitis due to a proved virus. One cannot successfully differentiate a "primary" from a "secondary" inflammation.

Dr. Kramer and Dr. Meyer have both stressed the fact that morphology can lead us astray. It has been our attempt to show that such words as toxic and degenerative are not agnostic enough, and that they preclude the possibility of bacteria or virus as the cause of a group of diseases that pathologically cannot be proved to be either degenerative or toxic.

Our plea has been merely that we should consider the diseases characterized by focal lesions in the white matter, as well as the diffuse types of encephalitis, as possible virus diseases, and that all effort should be made for transmission to animals.

DR. A. FERRARO, New York: In answer to Dr. Meyer's wishes, I am glad to state we have already tried some experimental work with the intention of reproducing measles in encephalitis in monkeys.

We have carried out two series of experiments, the first being represented by three monkeys into which intracerebral injections of human material have

been made. Of the three monkeys, only one showed symptoms pointing to a possible involvement of the central nervous system. We unfortunately waited too long, and the monkey recovered.

In the second series we have inoculated two other monkeys. One of them showed symptoms pointing to involvement of the central nervous system. This animal was killed just two days ago, so I am not now in a position to report on the histologic observations.

We realize the importance of experimental work, and whenever a favorable opportunity presents itself we shall inoculate other animals in order to establish the possibility of transmission.

# CEREBELLAR HEMANGIOBLASTOMAS WITH INCIDENTAL CHANGES OF THE SPINAL CORD

A CLINICOPATHOLOGIC STUDY \*

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The subject of hemangioblastoma has been amply discussed by Lindau,<sup>1</sup> and Cushing and Bailey<sup>2</sup> have reviewed the subject and the literature thoroughly in their recent book. It is not the purpose of this presentation to dwell on the histopathology of this type of tumor so much as on the diagnostic difficulties offered by the unusual associated changes of the spinal cord found in our material. The first case presented a clinical picture of multiple sclerosis which was recognized early. Syphilis of the central nervous system and tumor were also considered. In the second case, although a tumor was suspected, the unusual changes in the spinal cord suggested a degenerative or inflammatory disease of the cerebrospinal system. Aside from these observations, there are other interesting features which will be brought out in the report and discussion of the cases.

## REPORT OF CASES

CASE 1.—S. S., a Polish woman, aged 42, was admitted to the Montefiore Hospital on Jan. 20, 1928, complaining of visual impairment, diplopia and inability to walk. She had been well until about thirteen years before admission, when she began to see double, and experienced spells of dizziness and tinnitus; this condition lasted for six months. About a year later, vision began to be impaired, and reading became difficult. It would seem from the incomplete history that the double vision disappeared and reappeared irregularly. In January, 1925, she had difficulty in walking for about one year, and also some urinary urgency. In

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\* From the Laboratory of Neuropathology and the Neurological Division, Montefiore Hospital.

\* Read at the Fifty-Sixth Annual Meeting of the American Neurological Association, Atlantic City, N. J., June 9, 1930.

1. Lindau, A.: Studien über Kleinhirneysten: Bau, Pathogenese und Beziehungen zur Angiomatosis retinae, *Acta path. et microbiol. Scandinav.*, supp. 1, p. 1, 1926.

2. Cushing and Bailey: Tumors Arising from the Blood Vessels of the Brain: Angiomatous Malformations and Hemangioblastomas, Baltimore, Charles C. Thomas, 1928.

November, 1925, she vomited for a period of two weeks, and was dizzy on rising from bed or elevating her head. At that time, a neurologic examination revealed a right optic atrophy, bilateral signs of the pyramidal tracts, absent vibratory sense up to the hips, a right supranuclear facial palsy and horizontal nystagmus.

About nine years after the onset, the right lower extremity became stiff. Gradually both lower extremities became weaker, and she found walking extremely difficult. During all these years she had received antisyphilitic therapy irregularly.

The family history, with the exception that her father had died of a malignant gastric condition at the age of 58, was without significance. She married at the age of 20, was pregnant seventeen times, and had six children, all of whom were living and well. The other pregnancies were all terminated prematurely by mechanical means. The husband was living and well. She had had the usual infectious diseases of childhood, which were uncomplicated.

In August, 1927, the following conditions were noted at the outpatient department of the Neurological Institute: she walked on a broad base and showed kinetic incoordination; there were bilateral signs of involvement of the pyramidal tracts, dilated pupils, horizontal nystagmus and pallor of the right optic disk; no mention was made of the left disk; sensory disturbances were not noticed. A diagnosis of multiple sclerosis was made.

On admission to Montefiore Hospital, general examination revealed a well nourished woman with poor dental hygiene. The blood pressure was 110 systolic and 80 diastolic.

*Neurologic Examination.*—The patient was unable to walk; she had slight ataxia of the limbs, pseudo-athetoid movements in the fingers, bilateral hyperreflexia, absent abdominal reflexes and extensor responses to plantar stimulation. Vibratory sense was lost up to and including the hips, and postural sense was impaired in the toes of both feet, more so on the right. The pupils were irregular, the left larger than the right, and reacted well in accommodation but poorly to light. There were bilateral external rectus weakness, horizontal nystagmus and a right supranuclear facial palsy. The fundi showed primary optic atrophy on the right with papilledema of from 5 to 6 diopters elevation on the left.

*Laboratory Data.*—Chemical analysis of the blood showed: sugar, 195 mg. per hundred cubic centimeters; urea nitrogen, 17.1 mg. The blood picture was normal. Lumbar puncture showed a clear fluid, which was free from albumin and globulin but contained on one occasion 54 cells, 59 per cent lymphocytes and 41 per cent polymorphonuclear leukocytes, and on another occasion 58 cells, 70 per cent lymphocytes and 30 per cent polymorphonuclear leukocytes. The urine showed a high specific gravity, no albumin, large quantities of sugar and a trace of acetone. The Wassermann reaction of the blood and spinal fluid was negative on repeated occasions.

*Course.*—Power in the lower limbs became more and more impaired. The urinary incontinence became complete and of the overflow type. The patient had frequent spells of vomiting and dizziness despite the fact that the diabetes was under control. The papilledema of the left disk varied between 4 and 5 diopters in elevation. On Feb. 24, 1928, roentgenograms of the skull showed no abnormalities, but a ventriculogram showed internal hydrocephalus with dilatation of the left lateral ventricle which was displaced slightly to the right of the midline. Caloric Bárány tests showed nothing that could be considered abnormal. In time she became completely bedridden, and severe bed sores developed. On June 25, another spinal tap showed no cells with a 1 plus test for globulin and albumin. A later specimen showed a total protein of 57.8 mg. per hundred cubic

centimeters. The serology was negative on all occasions. She gradually assumed the position of paraplegia in flexion. The last status showed nystagmus in all directions and irregular pupils, which reacted poorly to light and better in accommodation. The old features persisted, except that it was difficult to elicit the knee reflexes as actively as previously because of the position of the lower limbs. The heart rate was rapid (126 per minute), and the blood pressure was 110 systolic and 90 diastolic. A perimetric field examination could never be done because of poor cooperation. The outstanding mental condition was one of

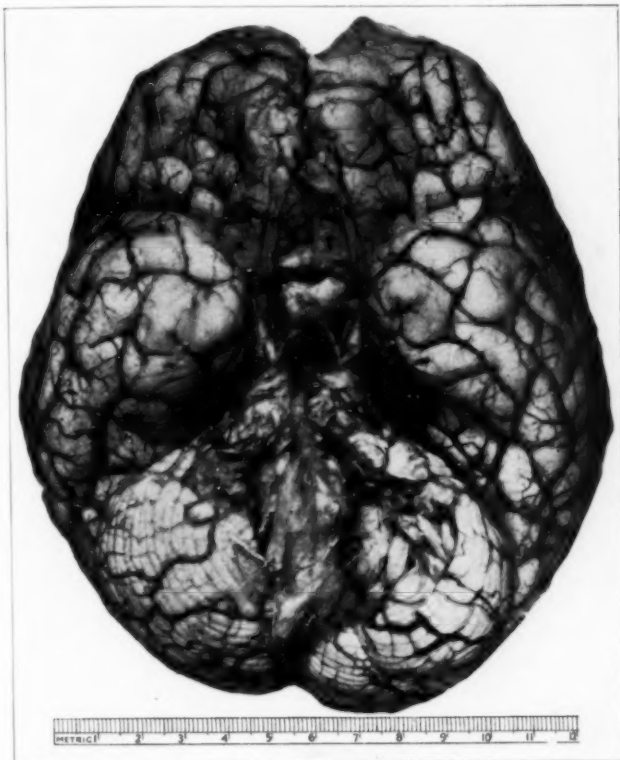


Fig. 1 (case 1).—Posterior view of the cerebral hemispheres, showing an opening in the left cerebellum through which cerebrospinal fluid escaped.

euphoria and lack of insight. When asked how she was during her worst states, she would almost invariably say "all right." She was quiet, cooperated poorly, and had some slight memory defects for recent events. She had an irregular temperature. Toward the last few weeks of life her condition was low, the pulse was rapid, she ate poorly, and she vomited occasionally. The blood sugar varied between 87 and 210 mg.

*Diagnosis.*—The clinical diagnosis was multiple lesions of the cerebrospinal system due to syphilis. Multiple sclerosis was considered, and the remote possibility of an infrafrontal neoplasm, possibly a gumma, was mentioned.



Fig. 2 (case 1).—Coronal section of the brain through the atrium ventriculi, showing a dilatation of the posterior horns of the lateral ventricle. Note the left cerebellar cyst and displacement of the aqueduct of Sylvius to the right.

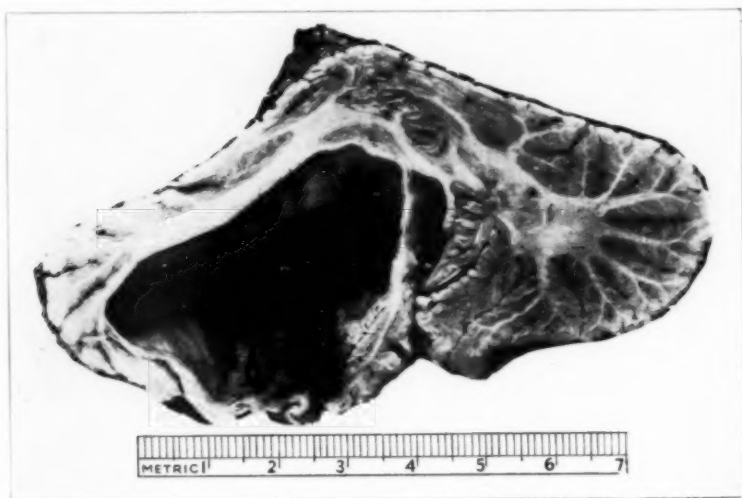


Fig. 3 (case 1).—Cerebellar cyst with mural tumor and displacement of the aqueduct of Sylvius.

*Necropsy.*—The right hemisphere of the brain appeared larger than the left, and there was greater flattening of the convolutions on the right. The pia-arachnoid of the interpeduncular space and the left cerebellum was markedly distended with fluid. The cerebellum was soft and had an opening through which cerebrospinal fluid escaped (fig. 1). The brain, when cut vertically, showed dilatation of the entire ventricular system (fig. 2). Throughout the centrum ovale there were small sclerotic plaques which were barely detectable with the naked eye.



Fig. 4 (case 1).—Hemangioblastoma, showing the lacunae lined by endothelial cells. Note the absence of a muscular coat in these vessels and the type of cells between the vascular channels. Hematoxylin and eosin stain;  $\times 150$ .

On cutting through the cerebellum there was found an encapsulated cyst containing a mural tumor, the size of a hazelnut, which was vascular. The entire left cerebellum was destroyed by the cyst, which pressed on the structures on the right and obstructed the aqueduct and the fourth ventricle (fig. 3).

The dura appeared normal. In the midthoracic region there was a slight, soft bulging of the spinal cord. Several segments were embedded in celloidin. A small portion of the swelling was preserved for fat stains.

*Microscopic Examination.*—Frozen sections of the tumor were stained by the hematoxylin and eosin, sudan IV, Perdrau and Cajal methods. Celloidin sections of the same material were stained by the hematoxylin and eosin, Mallory, and van Gieson methods.

With a low power lens the tumor mass showed numerous lacunae and cavernous sinuses which were lined by endothelial cells (fig. 4). Some of the sinuses were filled with blood and some with polymorphonuclear leukocytes, and others were completely empty. With the sudan IV stain, the tumor cells between the lacunae showed discrete fatty granules, called by Lindau xanthoma cells.

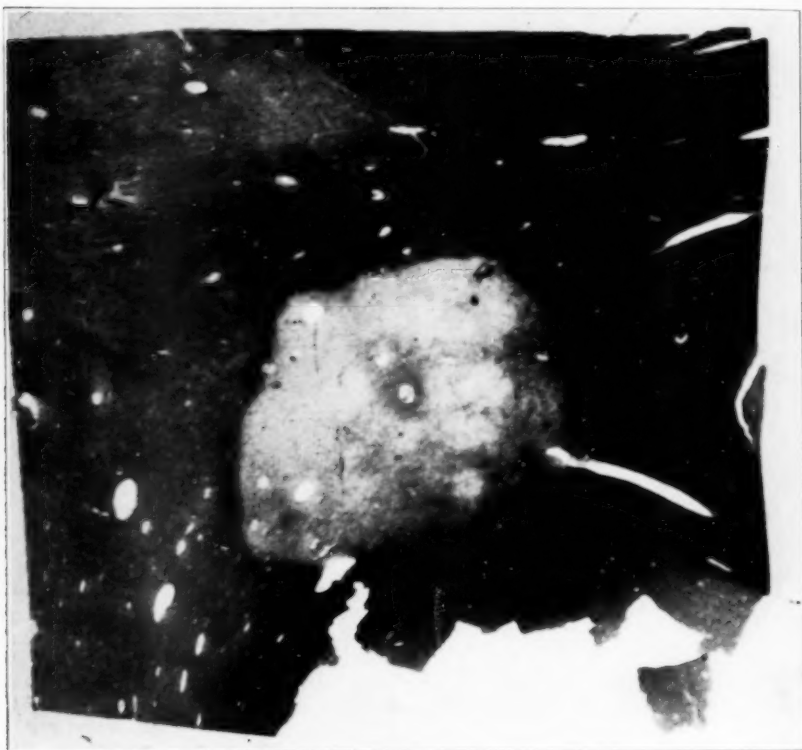


Fig. 5 (case 1).—Section of the centrum ovale, showing a sclerotic plaque. Weil stain;  $\times 25$ .

With hematoxylin and eosin the larger lacunae were cavernous; in them, beyond the endothelial lining, there was condensation of the collagen fibers. Between the lacunae the tumor was formed by numerous cells which varied in size, the nuclei of some being oval and vesicular, and of others irregular and staining deeply. The lining cells of some of the smaller capillaries were round and large and had pale nuclei which frequently protruded into the lumen of the capillaries, obliterating them. In places small homogeneous areas were found which took a colloid-like stain. Part of the cerebellum adjacent to the tumor mass showed signs of compression and destruction. Some of the Purkinje cells had undergone com-

plete degeneration, others showed atrophic changes, and some showed merely poor staining qualities of the Nissl substance. In places slight invasion by the tumor tissue could be observed.

The plaques in the centrum ovale consisted of demyelination of the white fibers (fig. 5) and proliferated glia fibers and nuclei.

In the region of the angle of the fourth ventricle of the medulla oblongata there was a distortion of the contour due to pressure, as well as demyelination



Fig. 6 (case 1).—Transverse section of the medulla oblongata at the crossing of the pyramids, showing a sclerotic plaque on the left involving part of the posterior column, substantia gelatinosa rolandi, part of the crossed pyramidal tract and fibers of the dorsospinocerebellar and rubrospinal tracts. Weil stain;  $\times 30$ .

of one of the pyramids and increase in the glia nuclei. The nerve cells of the nucleus cuneatus and substantia gelatinosa rolandi on the flattened side showed various changes from complete destruction to mild atrophy and poor staining of the Nissl substance. A section of the medulla at the crossing of the pyramids (fig. 6) showed an area of sclerosis involving the left crossed pyramidal fibers, as well as partial destruction of the substantia gelatinosa rolandi, and of fibers

of the dorsospinocerebellar and rubrospinal tracts. Under higher magnification the myelin sheaths of this area showed complete destruction. There were no evidences of Lueckenfeldern, and the vessels in this area were slightly thickened. There was an increase in the glial nuclei. With cresyl violet the nerve cells showed changes similar to those already described.

Sections were made at various levels of the spinal cord. At the eighth dorsal segment there was a complete demyelination of the right posterior column, and of the crossed pyramidal, Lissauer, rubrospinal and dorsospinothalamic tracts (fig. 7). The left posterior column was partially demyelinated, and the left pyramidal tract was spared. Under higher magnification the demyelination was

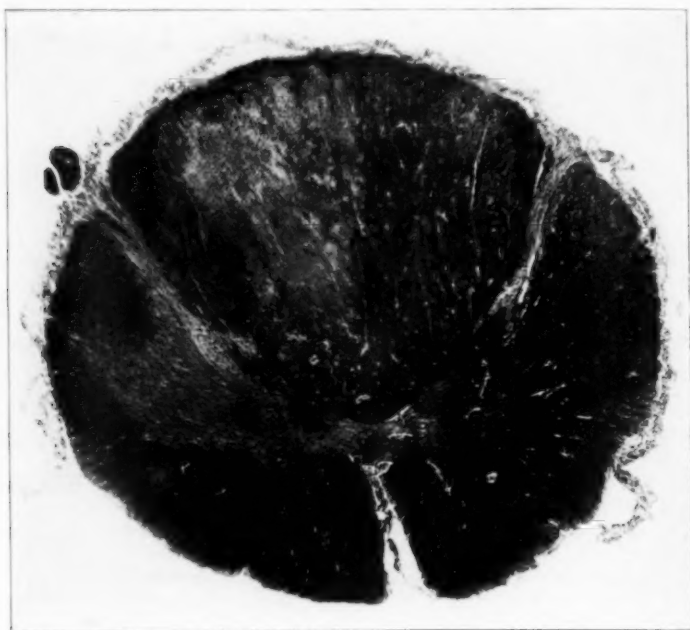


Fig. 7 (case 1).—Transverse section of the spinal cord at the eighth dorsal segment, showing destruction of the posterior column, and part of the right crossed pyramidal, Lissauer, rubrospinal and dorsospinothalamic pathways. Weil stain;  $\times 25$ .

fairly complete. The van Gieson stain showed endothelial proliferation of the capillaries and an increase in the glia nuclei. With Victoria blue the glial reaction was that seen in multiple sclerosis, i. e., condensation (fig. 8). With the Bielschowsky stain there was some alteration and destruction of some axis cylinders. Most of them were fairly well preserved (fig. 9). The nerve cells in the gray matter of the cord did not show any marked changes. The sections of the cord above this level showed merely an ascending type and those below a descending type of degeneration. At the eleventh and twelfth dorsal segments a few corpora amylacea were found within the pia-arachnoid.

*Microscopic Diagnosis.*—The diagnosis was: (1) hemangioblastoma of the cerebellum; (2) multiple sclerosis.

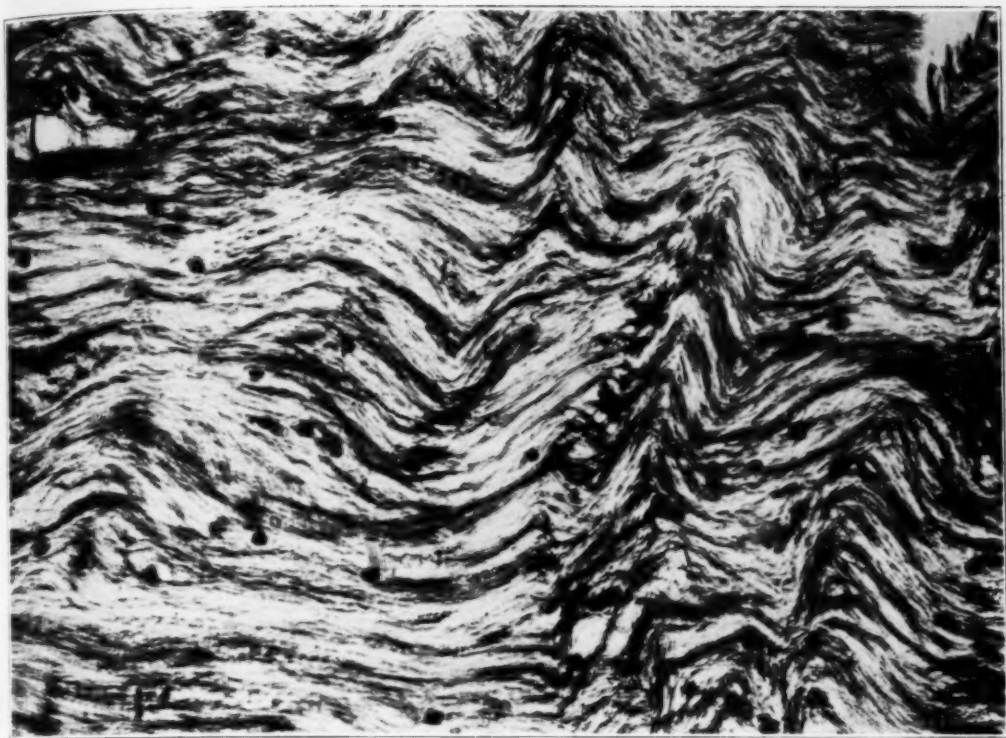


Fig. 8 (case 1).—Longitudinal section of the cord, showing condensation and undulation of glia fibers. Victoria blue stain; reduced from  $\times 400$ .

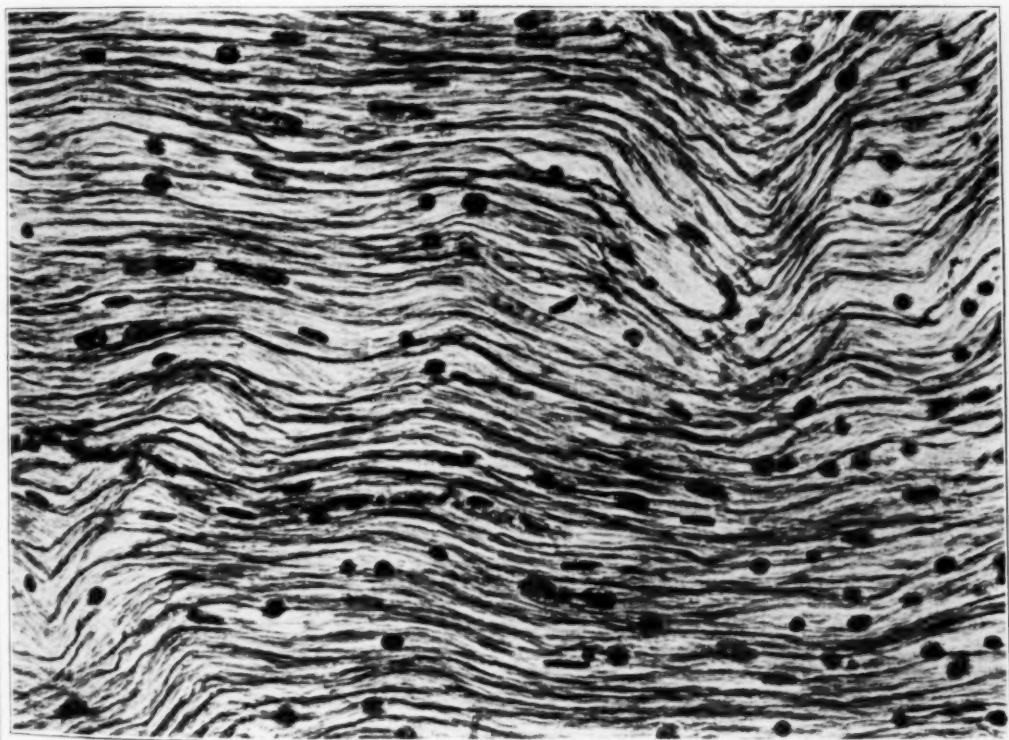


Fig. 9 (case 1).—Same section as figure 8, showing fairly well preserved axis cylinders with destruction of some from a multiple sclerotic patch. Bielschowsky stain; reduced from  $\times 400$ .

CASE 2.—S. B., a man, aged 44, was admitted to the Montefiore Hospital on Jan. 13, 1929. Approximately thirteen months before, he had become weak, and one day, on returning from business, he had vomited. Shortly thereafter he complained of drowsiness, anorexia, headache, vertigo and diplopia. He became very irritable. For one or two months in the early part of the illness he had an inversion of the sleep mechanism. Gradually the gait became unsteady, and he had to be supported to retain his equilibrium. For a period of three months during the illness he had stiffness of the muscles of the neck and experienced great pain on moving the head. This disappeared about ten months after the onset of the illness. Loss of libido and power of erection, as well as sphincteric difficulties, appeared in the early months of the illness. In June, 1928, he began to have difficulty in swallowing. He often regurgitated and choked on food. This defect had had remissions and exacerbations; shortly afterward, exophthalmos was noticed. In October, he was unable to walk or sit up. He lost weight and strength and in the few months before admission he coughed and expectorated a great deal.

*Physical Examination.*—The patient was poorly nourished and bedridden, and he cooperated with difficulty. His face was acrocyanotic. The eyes bulged somewhat. The chest was barrel-shaped. The spine was kyphosed. Râles were heard at the bases of the lungs. A moderate amount of peripheral vascular sclerosis was observed. The heart was normal. The blood pressure was 112 systolic and 70 diastolic. The prostate gland was enlarged.

*Neurologic Examination.*—There was general muscular atrophy, including the trunk; all muscle groups were correspondingly weak, but more so on the right. The tonus of the right upper extremity was increased and power was diminished. The deep reflexes were hyperactive throughout, greater on the right than on the left. There were bilateral Babinski and confirmatory signs. The abdominal reflexes were definitely diminished. Fibrillations were present in the pectorals, calf and thigh abductor muscles. Intention tremor of the left hand and past-pointing of about 2 inches in the right hand were observed. Sensory impairment to touch, pinprick, temperature, position sense and vibration was found in the right lower extremity. The fields showed no limitation grossly, and there was myopia of from 10 to 12 diopters. A slight amount of papilledema was present bilaterally. The pupils were equal and reacted to light and in accommodation. Convergence was poor. Horizontal nystagmus in both directions, as well as positive Stellwag and Moebius signs, was observed. The fifth nerve was normal except for right corneal hypesthesia. There was a right supranuclear facial palsy. The left side of the palate seemed paretic; the pharyngeal reflex was absent, and there was occasional hiccup. Respiration was sighing, and swallowing was difficult. The right sternocleidomastoid and trapezius were weak, and the chin tended to tilt to the right. The tongue deviated to the right.

*Course.*—The condition became poorer. The state of the fundi was questionable because of the high degree of myopia. The picture varied from slight edema or hyperemia to an elevation of 1 and possibly 2.5 diopters in the left eye.

*Laboratory Data.*—With the exception of a leukocytosis (12,400) all laboratory data as well as manometric tests were normal. The labyrinthine reactions were normal. Roentgen examination of the skull gave negative results. A roentgenogram of the spine showed a narrowing of the body of the eighth, ninth and tenth dorsal vertebrae with deformity and sclerosis of the body (fig. 10) and lateral ligaments (kyphosis had been noted in this region); loculations and trabeculations were not found; the plate had the appearance of an old Pott's disease.

*Clinical Diagnosis.*—The diagnosis was: a diffuse degenerative or inflammatory process of the cerebrospinal system. Tumor of the posterior fossa was considered.

*Necropsy.*—The right lobe of the cerebellum showed an area of depression. At the right cerebellopontile angle there was a firm tumor, extending from the lower third of the pons to the lower portion of the medulla oblongata, which was



Fig. 10 (case 2).—Roentgenogram, showing narrowing and sclerosis of the bodies of the eighth, ninth and tenth dorsal vertebrae.

partially adherent to the eighth nerve and to the fibers of the ninth and tenth cranial nerves. The brain was cut vertically. The entire ventricular system was slightly dilated. The diencephalon showed a certain amount of flattening as a result of pressure by the tumor. The same was true of the structures of the midbrain. When the pons and cerebellum were cut, the fourth ventricle was dilated and distorted in its upper portion. The vessels at the base of the brain were markedly congested and showed evidence of subarachnoid hemorrhage. The

sections at the level of the eighth nerve showed a distortion of the medulla oblongata and pons. In the vicinity of the medulla oblongata the tumor was somewhat encapsulated; on cutting, it was found to be hemorrhagic; it had a semigelatinous, buttery consistency and presented numerous small lacunae.

The spinal cord was of unusually large diameter throughout. On palpation no areas of softening could be made out. The area adjacent to the tenth thoracic segment of the cord showed a slight area of softening. In the thoracic and lumbar portions there was a definite destruction involving the anterior portion of the cord and the gray matter mainly. Segments of the cord at various levels were embedded for further histologic study.

*Microscopic Examination.*—The tumor presented a picture typical of hemangioblastoma as described in case 1, with the exception that there was no cyst (figs. 11 and 12).

*Diagnosis of Tumor.*—The diagnosis was hemangioblastoma of the cerebellum.

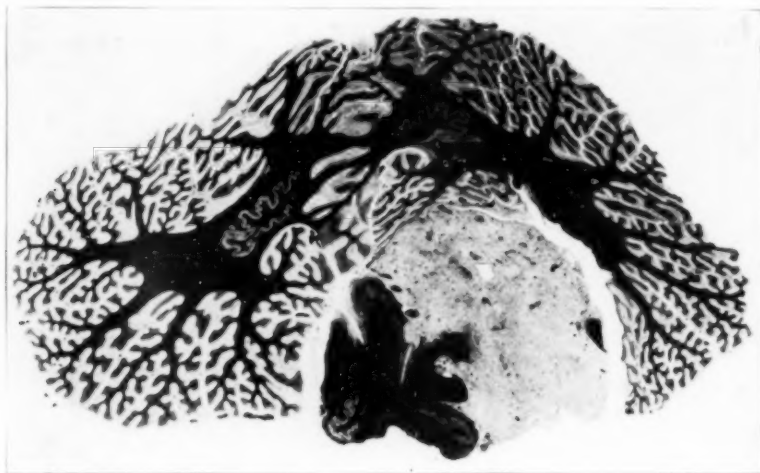


Fig. 11 (case 2).—Section of the cerebellum, showing a solid tumor on the right causing destruction of part of the right cerebellum and marked compression of the medulla oblongata. Weil stain;  $\times 2$ .

Sections of the cerebellum and medulla oblongata, as well as sections of the cord at various levels, were embedded in celloidin and stained by the Weil, hematoxylin and eosin, cresyl violet, van Gieson and Perdrau methods.

Sections of the cerebellum and medulla oblongata stained with the Weil method showed distortion of these structures with displacement of the superior olive to the right. On the left, part of the vermis and lateral lobe of the cerebellum was completely destroyed. With a lower magnification the pyramids were not only distorted but stained somewhat poorly. The lemnisci also showed some evidence of compression. With a higher magnification the pyramids showed a sievelike appearance, and in places the myelin sheaths showed mild destruction.

With hematoxylin and eosin and cresyl violet methods, the nerve cells of the ninth, tenth, eleventh and twelfth nerve nuclei showed changes of a mild degree. Some were slightly swollen and had an eccentrically placed nucleus and poorly stained Nissl substance. Others were shrunken and had a granular and fibrillary

appearance. The latter were smaller than normal, and some stained more deeply with cresyl violet; others, fewer in number, showed complete disintegration. Satellitosis and neuronophagia of some of the nerve cells were also observed. However, the majority of the nerve cells of these cranial nerve nuclei were normal in appearance. Some of the Purkinje cells in the area contiguous to the compression showed changes similar to those described.

Sections of the medulla oblongata at the decussation of the pyramids showed destruction like that just outlined with paling of the pyramids. The nerve cells

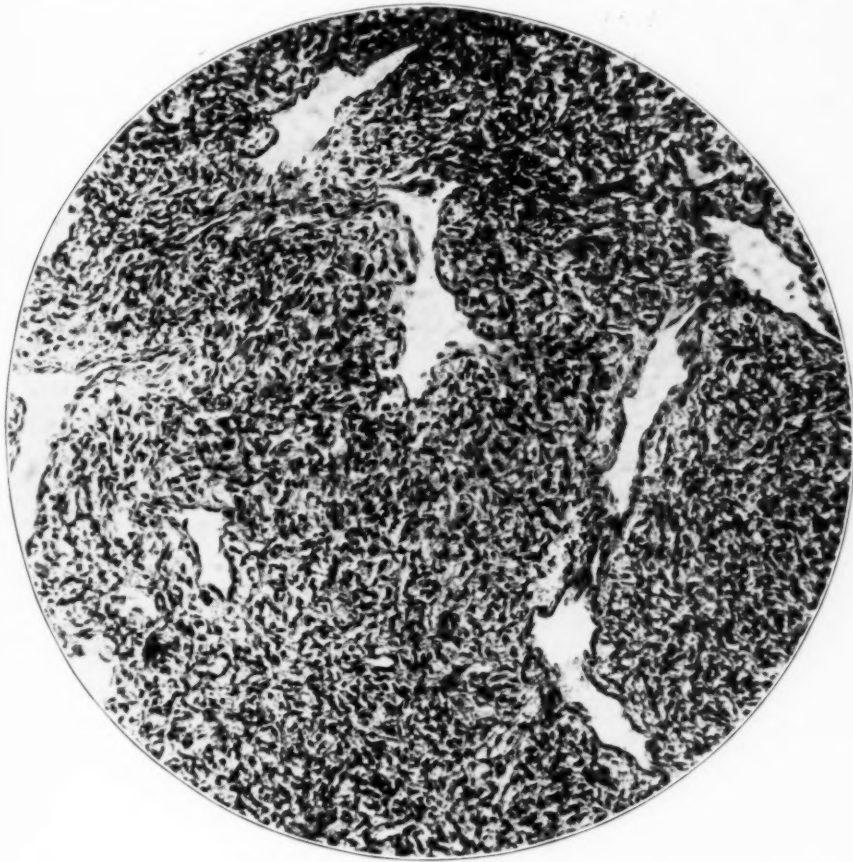


Fig. 12 (case 2).—Section of a hemangioblastoma, showing somewhat similar features as figure 4. Hematoxylin and eosin stain; reduced from  $\times 150$ .

of the hypoglossal nucleus in this area showed more marked changes and some complete disintegration. The anterior horn cells of the cervical portion of the cord showed changes, such as atrophy and loss of Nissl substance, and in places complete destruction.

With the Weil method, all sections of the spinal cord showed a slight marginal pallor, which involved the dorsal and ventral cerebellar pathways chiefly, and also the crossed pyramidal tracts. However, with a higher magnification these changes

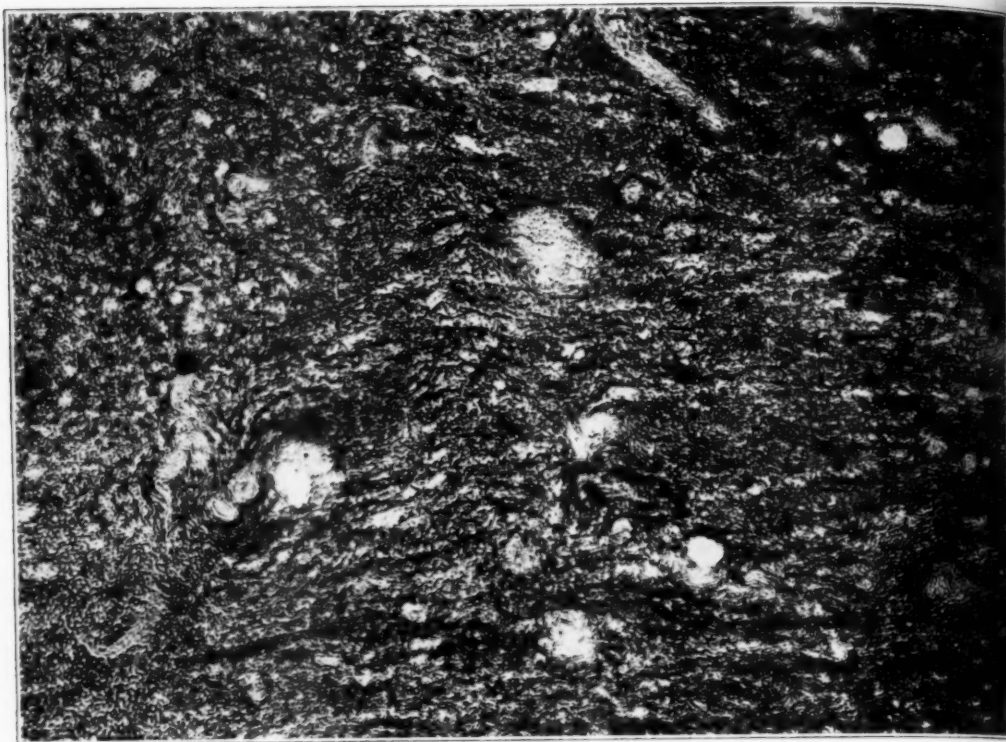


Fig. 13 (case 2).—Section of the cord, showing necrotic foci. Weil stain; reduced from  $\times 150$ .



Fig. 14 (case 2).—Same section as in figure 13, showing elements of one necrotic focus. Hematoxylin and eosin stain; reduced from  $\times 300$ .

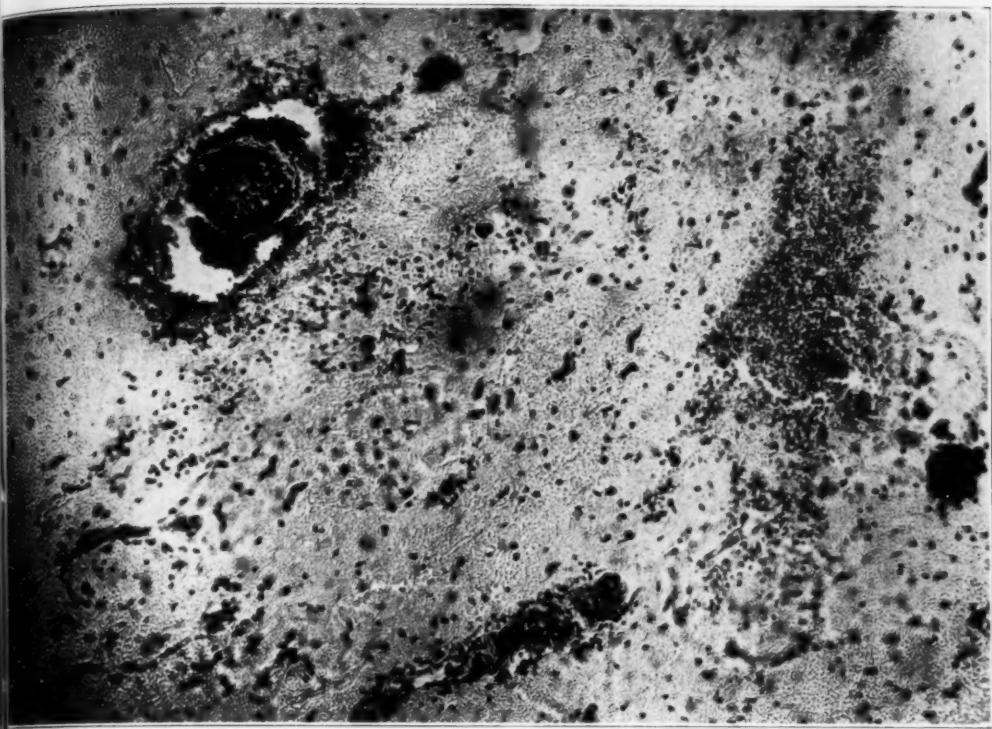


Fig. 15 (case 2).—Hemorrhage and extravasation of blood in the gray matter. Hematoxylin and eosin stain; reduced from  $\times 150$ .

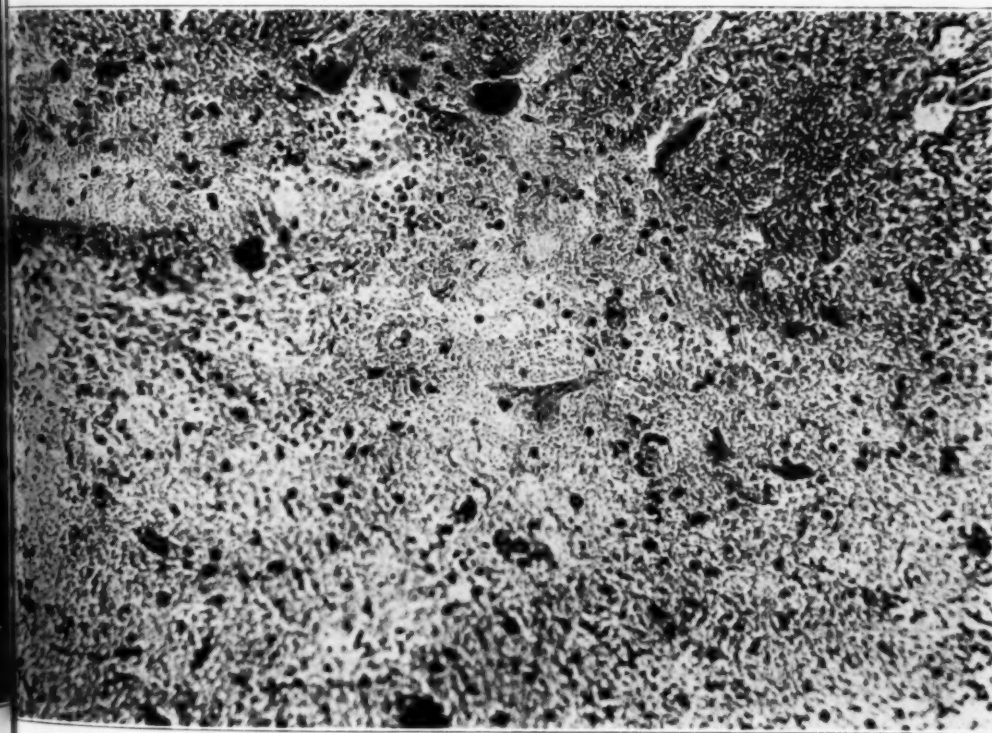


Fig. 16 (case 2).—Area of the gray matter, showing destruction of the anterior horn cells with preservation of a few. Cresyl violet stain; reduced from  $\times 240$ .

were not as marked, and only occasionally could swelling and destruction of the myelin sheaths be noticed. Throughout the cord there were patchy areas of destruction which had the appearance of artefacts with a very low power (figs. 13 and 14). Nevertheless, under a higher magnification these necrotic areas consisted of a fine reticulum which contained elements allied to the compound granular corpuscles (fig. 14). Most of these lesions were confined to the crossed pyramidal and to the vicinity of the spinothalamic tracts. These were mostly observed in the dorsal segments and were more marked at the levels between the eighth and eleventh dorsal segments. At the eighth dorsal segment a few of these necrotic foci were also observed in the gray matter. At the tenth dorsal segment there were marked destruction of the gray matter, hemorrhage, extravasation of red blood cells, an accumulation of pigment and a few compound granular corpuscles (fig. 15). The nerve cells of the anterior horns at this level had undergone pathologic changes in the nature of shrinkage, disappearance of the Nissl substance, satellitosis and neuronophagia, as well as complete destruction of some cells (fig. 16). The glial elements within this region were increased.

A similar area of involvement was also found in the right posterior horn of the gray matter of the tenth dorsal segment, but this was not as extensive as the one found in the anterior horn of the same segment. The Virchow-Robin space of one of the vessels in this region showed an apparent accumulation of round cells, which were, however, none other than gitter cells. A lesser destruction of gray matter was observed in the third, fourth, fifth and sixth dorsal segments, especially in the vicinity of the posterior commissure. The detailed microscopic picture of these changes was similar to that already described. In the lumbar and sacral regions the changes were not as marked, and at the third sacral segment a few vessels in the gray matter showed an accumulation of what appeared to be round cells.

*Microscopic Diagnosis.*—The diagnosis was: (1) hemangioblastoma of the cerebellum causing compression of the medulla oblongata; (2) degeneration of the spinal cord throughout its axis (etiology unknown).

#### COMMENT

Clinically, in its early stages, case 1 presented the history and neurologic appearances of multiple sclerosis. There is reason to believe that the neoplasm, although not suspected until 1928, had been present for a long time, as is common in this condition. It must have been there since November, 1925, when the patient had attacks of vomiting and right optic atrophy, although nothing was said of the condition of the left fundus until 1928, when an elevation of from 4 to 5 diopters was noticed. Then a diagnosis of right infrafrontal neoplasm was made because of the presence of a Kennedy syndrome, an error frequently made in tumors of the posterior fossa. In view of the observations, the euphoria is easily explainable on the basis of multiple sclerosis.

It is believed that the symptoms and signs in this case were primarily due to the neoplasm. The histopathology of the tumor conformed to the description given by Lindau, although the retina and other organs were free from these cysts. Cushing and Bailey agree that a true hemangioblastoma may be found in the cerebellum without other like lesions being present elsewhere in the body.

Aside from the tumor, the case presented a definite histopathologic picture of mild multiple sclerosis, with the greatest involvement in the eighth dorsal segment. There were small multiple patches throughout the cerebrospinal axis. On account of the ascending and descending degeneration of the columns of the cord, we thought at first that we were dealing with some level lesion due to softening. A careful study of the spinal cord at this level with the Weil, Victoria blue and Bielschowsky stains, however, showed the picture of multiple sclerosis. Ascending and descending degeneration of the fiber tracts of the cord, although rarely observed in this disease, can be conceived of when there is destruction of the axis cylinders. The small sclerotic plaques found in the medulla oblongata and throughout the centrum ovale confirm this impression.

However much one may be tempted to try to separate the signs of tumor from those of multiple sclerosis, it is obvious that the attempt must prove unsatisfactory and inconclusive at best. Although such consideration may prove of academic interest, it cannot throw sufficient light on the subject to prove to our satisfaction, even at present, that there was not enough reason to abstain from operative intervention.

From a therapeutic point of view, this is the type of case that teaches very little, for one is inclined to believe that were a like syndrome to repeat itself, hesitation and doubt concerning both diagnosis and treatment would possibly still be as great; however, one might suspect the various possibilities. What active measures are indicated in the presence of papilledema and ventriculographic evidence of marked dilatation of the entire ventricular system, when this is accompanied by definite disease of the spinal cord, is a moot question.

In case 2 the history impresses one with the possibility of a cerebral neoplasm. The neurologic data pointing to a diagnosis of neoplasm of the posterior fossa were many, but these were overshadowed by the observation of muscular atrophy, fibrillation and evidences of sensory abnormalities limited to the right lower extremity. On account of these complicating features, there was a divergence of opinion; some regarded the condition as an encephalomyelitis, others as diffuse degenerative disease of the cerebrospinal axis; others again considered the possibility of a neoplasm of the posterior fossa. The changes in the fundi could not be relied on because of the high grade myopia. The roentgen observations in this case were not sufficiently stressed—the roentgenologist first reporting an involvement of the ninth dorsal vertebra and attributing the changes to Pott's disease. A later review of the roentgenograms by us and the roentgenologist, in the light of the cerebellar pathology, revealed destruction of the eighth, ninth and tenth dorsal vertebrae (fig. 10) such as is seen in metastatic tumors.

As was pointed out by Bailey and Bucy,<sup>3</sup> Guillain, Decourt and Bertrand,<sup>4</sup> Makrycostas<sup>5</sup> and others, a number of these cases reported as Pott's disease or metastases to the vertebrae were found to be the seat of hemangiomas causing compression of the cord. We were not fortunate enough to secure specimens from the diseased vertebrae for further study, but we think that the changes in these could not have been due to any metastatic tumor, for a careful search of the organs did not reveal any primary neoplasm with the exception of the cerebellar hemangioblastoma. In reviewing the literature, Bailey and Bucy<sup>3</sup> stated that twenty-seven cases of hemangioma of the vertebrae have been reported. Eleven were associated with clinical symptoms and sixteen were found at autopsy with antemortem indication of their presence. The clinical symptoms were those of compression of the spinal cord in ten of the eleven cases. The pathologic process consisted of numerous groups of cavernous vascular channels and absorption and deposition of bone.

The histopathologic observations were twofold: (1) a right cerebellar hemangioblastoma without a cyst, causing destruction of the cerebellum and severely compressing the medulla oblongata and cervical portion of the spinal cord, and (2) changes in the spinal cord throughout with major changes in the segments from about the eighth to the eleventh dorsal. How many of these changes were due to compression is difficult to state. The nonuniformity of the pathologic changes causes some doubt as to the exact nature of the etiologic factors. The necrotic focal areas were at first thought to be due to some functional circulatory interference. Changes in the walls of the vessels were, however, not found. The process, especially in the tenth dorsal segment, was more akin to that observed in trauma to the cord. Whether or not the vertebral pathologic condition caused compression of the cord and acted as trauma is difficult for us to state definitely.

The atrophy of the muscles of the upper extremities was partly due to distortion of the cervical portion of the cord and some secondary changes in the anterior horn cells, such as were described in the lower dorsal segments. The changes in the anterior horn cell in the rest of the segments were analogous in a lesser degree to those found between the eighth and the eleventh dorsal segments.

We wonder, in retrospect, whether a more careful consideration of the vertebral roentgenograms would have made us any wiser during the life of the patient. Our roentgenologist stresses the fact that the

3. Bailey, P., and Bucy, P. C.: Cavernous Hemangioma of the Vertebrae, *J. A. M. A.* **92**:1748 (May 25) 1929.

4. Guillain, G.; Decourt, J., and Bertrand, I.: Compression médullaire par angiome vertébral, *Ann. de méd.* **23**:5, 1928.

5. Makrycostas, K.: Ueber das Wirbelangiom-Lipom und -Osteom, *Virchows Arch. f. path. Anat.* **265**:259, 1927.

plates showed nothing distinctive of osteal angioma; neither was there present anything which tended to rule out its possibility. It is likely that we might have thought the cerebral pathologic changes metastatic if we had been led at the time to think more carefully on the matter. In any event, the diagnostic difficulties presented by this case were so great that we fail to see how a diagnosis could have been made during the patient's life which would have led to operative intervention and possible benefit.

#### GENERAL COMMENT

Eleven cases of hemangioblastoma reported by Cushing and Bailey showed gradations from the simple capillary forms of tumor to the cavernous and cellular form. These investigators came to the conclusion that no tumor is architecturally pure in type. These tumors were all confined to the cerebellum and seven of them were cystic, the tumor mass expressing itself as a mural attachment. One of our tumors was cystic, the other was not. Lindau discovered that these cysts are frequently associated with retinal angiomas and with cystic anomalies in other organs of the body. In the eleven cases reported by Cushing and Bailey, case 19 showed the presence of an angioma of the retina. Our cases did not show cystic anomalies of any of the organs, unless the roentgen changes in case 2 are accepted as being hemangiomas. We are inclined to agree with Cushing and Bailey's conclusions to the effect that cerebellar cysts may occur without similar anomalies in other organs.

In case 2 the symptoms were noticed thirteen months before admission. In the cases reported by Cushing and Bailey the onset of symptoms before admission varied from two months to one year, with the exception of case 2, in which the symptoms were observed for four years; case 4, in which the symptoms were observed for a period of from two to nine years, and case 10, in which the patient had been a life-long sufferer from occipital headaches, the symptoms becoming aggravated three years before admission.

Unlike our cases, none of those reported by Cushing and Bailey showed changes in the spinal cord. Cases 19 and 20 of the Cushing and Bailey group showed unilateral astereognosis, and at one time each was suspected of being one of a lesion of the opposite cerebrum. In case 20 the parietal lobe was explored. They attributed the astereognosis to pressure by the tumor on the upper portion of the spinal cord. Beyond compression of the upper portion of the cord, none of the cases presented neurologic signs which could be attributed to diffuse lesions of the central nervous system, especially of the cord. When we consider the fact that these hemangiomas are benign tumors, it is unfortunate that our cases presented lesions distributed over the

entire cerebrospinal axis, throwing such doubt on the diagnoses that it seemed unwarranted even to consider operative intervention. This is especially deplorable when one realizes the relatively excellent prognosis that such operative procedures offer.

#### CONCLUSIONS

Two cases of cerebellar hemangioblastoma with some unusual changes in the spinal cord, which led to difficulties in diagnosis and especially in therapeutics, are presented.

Case 1 was complicated by the presence of multiple sclerosis. A careful study of the changes in the cord in case 2 has not brought us to a conclusion regarding its etiology.

It is thought that when a cerebellar neoplasm is suspected, in spite of other changes in the central nervous system, a suboccipital exploration should be made.

## PRIMARY MELANOBLASTOSIS OF THE LEPTOMENINGES AND BRAIN \*

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Primary melanoblastosis of the meninges is not unknown, but the number of cases recorded is rather small. Though the case here reported, like the instances previously described, offers no diagnostic criteria that would aid in identifying the condition during life, the rarity and the academic significance of this type of lesion justify a more detailed description of the anatomic and clinical manifestations.

### RECORD OF CASE

*Clinical History.*—E. G., a youth, aged 16, was admitted to the Providence City Hospital because of repeated epileptiform attacks, associated with headache and fainting spells, during the preceding six months. He was the youngest of a family of three. An older sister ran away from home and an older brother was in a reformatory school. The father died of tuberculosis; the mother was alive and well. The birth of the patient was at full term and uneventful. While physical development was apparently normal, he early displayed emotional and intellectual disturbances. He made fair progress at school. He spent several years in an orphanage. At the age of 13, while in the sixth grade at school, he began to manifest more serious irregularities of conduct. He was caught several times stealing minor objects; he was finally arrested in the act of stealing a bicycle and was committed to the reformatory. He remained there for one and a half years and then was paroled to the mother. Six months later, having broken his parole, he returned to that institution for the second time. He soon began to complain of severe headache and became subject to repeated fainting spells and vomiting. In the course of several weeks these attacks took the character of generalized convulsions, which were preceded by projectile vomiting. The condition remained unchanged for a period of ten days, and there were no further alterations in the mental or physical condition until about five days prior to transfer to the City Hospital. Then he became drowsy, and his temperature rose to 101 F. A lumbar puncture was performed; the cerebrospinal fluid, obtained under normal pressure, was xanthochromic and contained 6 cells per cubic centimeter. Wassermann tests of the cerebrospinal fluid and blood were negative. He was sent to the

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City Hospital with a provisional diagnosis of either acute epidemic encephalitis or some form of meningitis.

*Examination* (in the City Hospital).—The patient was drowsy, but could be aroused. He complained of severe frontal headache which, he said, was intensified by talking. He was somewhat confused but apparently well oriented. He was well developed and well nourished, and showed no deformities. There were many pigmented moles which varied in size and were distributed irregularly over the trunk and legs. No masses were felt in the abdomen. The chest revealed no abnormalities. A brownish-red secretion was noted in the nostrils, but no bleeding



Fig. 1.—Drawing showing the pigmentation of the leptomeninges at the base of the brain and the enlarged cisterna magna (C M.) forming a pseudocyst.

areas were discovered. The pupils were equal and 3 mm. in diameter; they reacted well to light and in accommodation. There was no nystagmus; the ocular excursions were within normal limits. The fundi were normal. There was a right supranuclear facial weakness. The deep reflexes in the upper extremities were active and equal. Both knee and ankle jerks were markedly depressed. There was bilateral ankle clonus, but no other pathologic reflexes were found. The abdominal reflexes were diminished, and the cremasteric reflexes were not elicited. Gait was normal. There was no ataxia, adiadokokinesis, dysmetria or sensory disturbances. Speech was intact.

*Course.*—During the first week at the hospital he had no convulsive seizures, but continued to have severe headache with projectile vomiting, and showed a gradual decline in mentality. At the end of the second week he became disoriented, apathetic and disinterested. The pupils became unequal, the left larger than the right (the right was now reduced to 2 mm.). The facial paresis now involved all three branches. The tongue deviated to the right. The knee jerks were still diminished, but were unequal, the right being more active than the left. The ankle clonus had disappeared, and a fine tremor of the left arm had appeared.

Repeated lumbar punctures were performed, and in each instance xanthochromic fluid, under normal pressure, was obtained. Each lumbar puncture and withdrawal of fluid was followed by intensification of the headache and by the

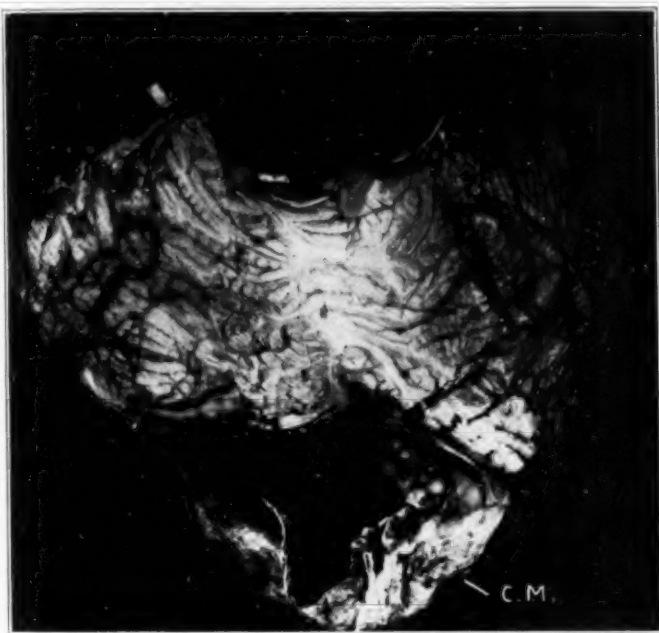


Fig. 2.—Photograph illustrating the partially collapsed cisterna magna (compare with fig. 1).

appearance of new neurologic signs. The convulsive seizures became more frequent; speech became inarticulate; the right eye became fixed in a position indicating complete external ophthalmoplegia; the general condition declined.

Operative intervention was thought to be inadvisable because of the poor physical condition of the patient. The disks, which were normal throughout the previous course, forty hours before death began to show swelling of the nerve heads.

During the terminal hours of the illness, there was a further decline. Speech became anarthric, and dysphagia appeared. The right eyeball, which previously had been fixed in a central position, became displaced medially. The left upper and both lower extremities were in flaccid paralysis; all deep reflexes and the abdominal reflexes disappeared.

Bronchopneumonia was the cause of death.

*Diagnosis.*—The condition was diagnosed as a tumor of the posterior fossa. Tuberosus sclerosis was also considered as a diagnostic possibility.

*Necropsy.*—General Examination (by Dr. H. Everett Smiley, Providence, R. I.): The body showed numerous irregularly scattered pigmented moles over the trunk and extremities. The pupils were unequal, the right measuring 6 mm. and the left 4 mm. in diameter. The peritoneal cavity was free from fluid and adhesions. The appendix and mesenteric lymph nodes showed nothing of note.

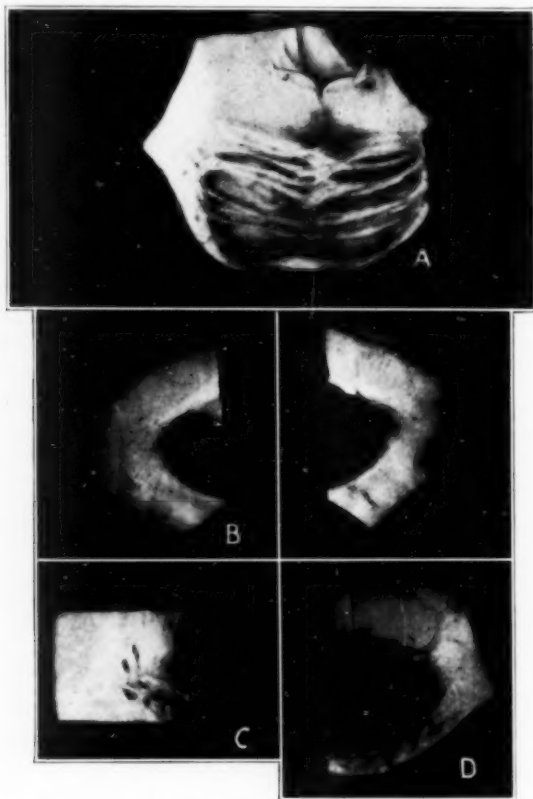


Fig. 3.—Photograph illustrating the infiltration of the pons and other parts of the brain by pigment material. A, pons; B, temporal poles; C, dentate nucleus, and D, pons.

The diaphragm reached the fifth space on each side. Both pleural cavities showed fibrous bands at the apex. There was no fluid in either cavity. The pericardial cavity was free from excessive fluid; there were no adhesions. The heart weighed 200 Gm.; all valves were normal. The right lung weighed 340 Gm., and the left lung, 345 Gm. Both lungs presented the picture of a terminal diffuse bronchopneumonia. The spleen weighed 60 Gm.; it showed no gross alterations. The liver weighed 1,050 Gm.; it was firm and otherwise normal. Each kidney weighed 100 Gm.; they appeared normal.

**Gross Anatomy of the Brain:** The brain weighed 1,480 Gm. It was somewhat injected. The ventral surface of both cerebellar lobes was covered by a thickened pia-arachnoid. This thickening extended to the region of the cisterna magna and down over the cervical segments of the spinal cord. The thickened meninges were of a brownish black color and firm consistency (fig. 11) and covered also the ventral surface of the medulla, pons and interpeduncular space as far as the anterior aspect of the chiasma. In the region of the cisterna magna there was a large cystlike expansion, the size of a baseball, filled with a brownish, thick fluid. This pseudocyst (fig. 1) collapsed on removal of the brain and was found to be

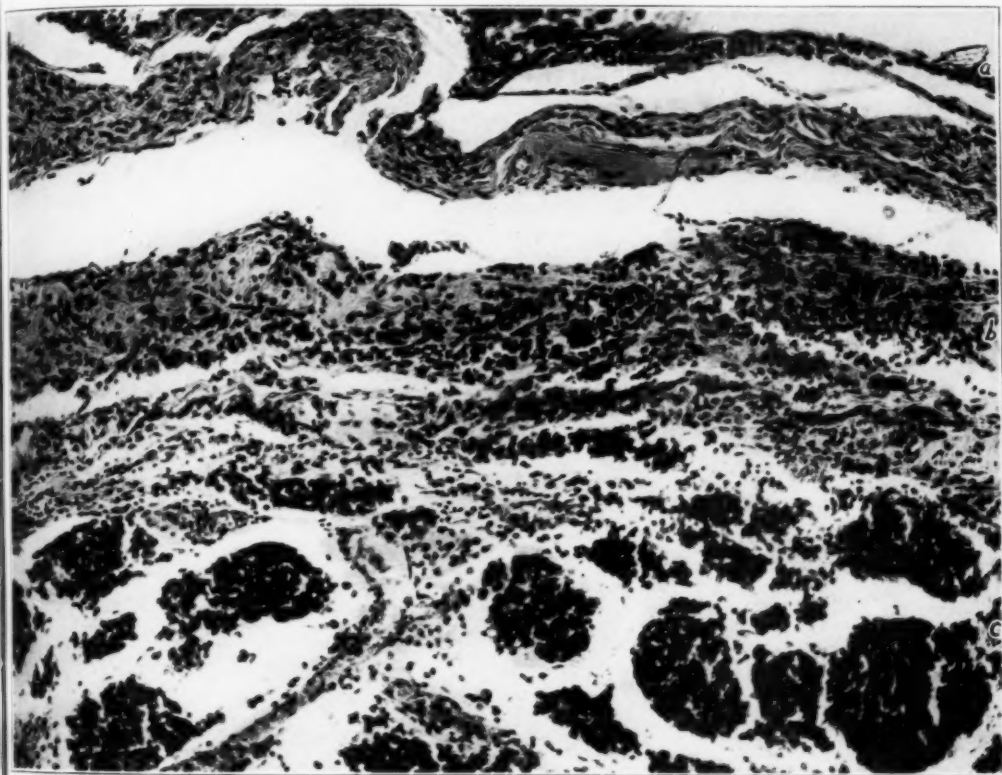


Fig. 4.—Photomicrograph illustrating the three zones in the infiltrated leptomeninges: *a*, pigmented layer; *b*, fibroblastic layer, and *c*, alveolar layer.

little more than an expanded cisterna magna (fig. 2), bounded by thickened and infiltrated arachnoid. The left lobe of the cerebellum was somewhat distorted and appeared softer than the right. The right lobe was unaltered.

There was a bilateral symmetrical hydrocephalus, involving all ventricular compartments. Cross-sections of the pons revealed a streaked appearance produced by strips of brownish-black pigmented tissue (fig. 3 *A*). In other areas, the pons showed more massive accumulation of pigment (fig. 3 *D*). Similar patches of pigment material were also found in the temporal lobes (fig. 3 *B*) and in other areas of the cerebellum and cerebrum (fig. *C*).

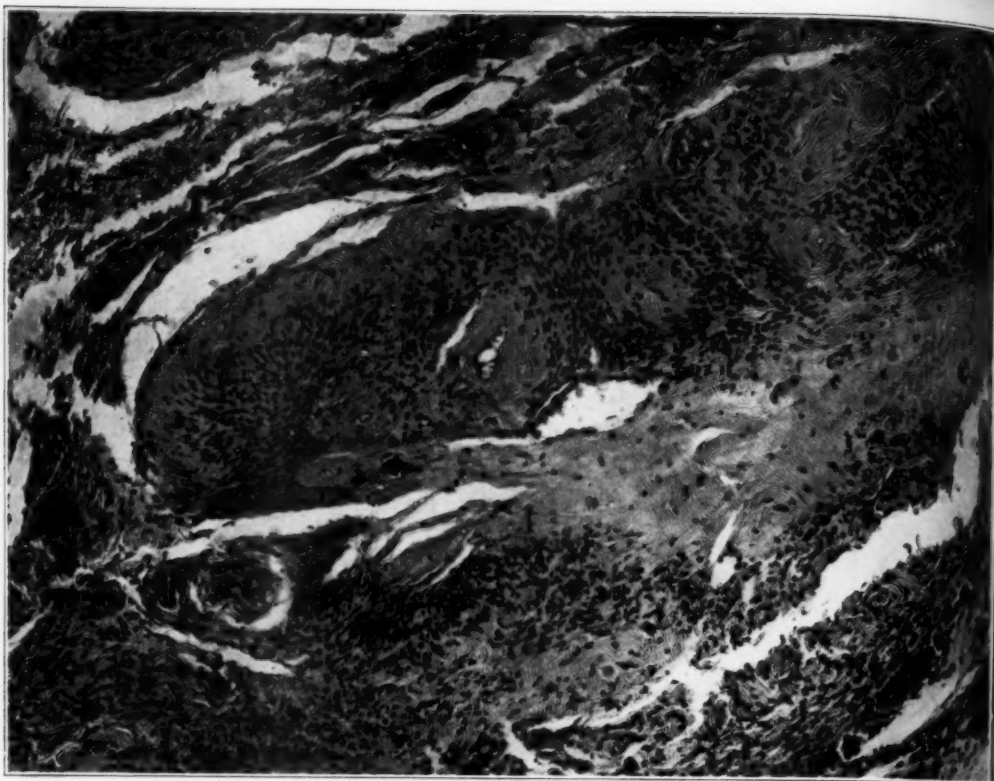


Fig. 5.—Photomicrograph illustrating the whorl-like cellular arrangement in the second zone.

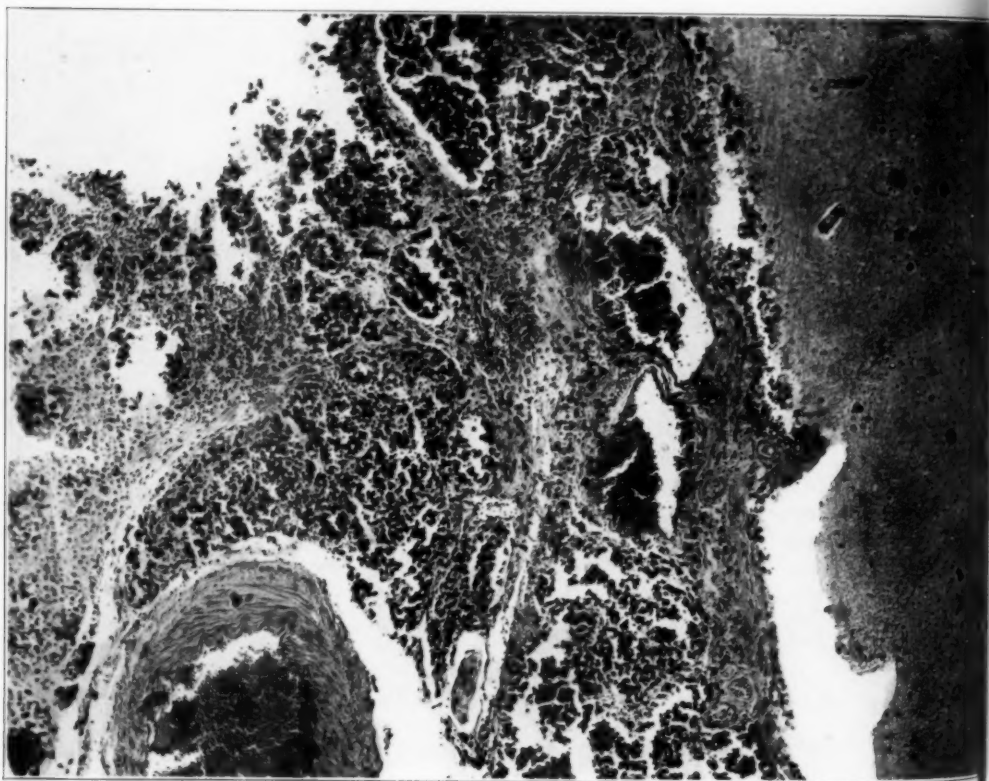


Fig. 6.—Photomicrograph, illustrating the markedly thickened leptomeninges on the ventral surface of the pons, with the alveolar zone forming the main infiltrating element.

*Microscopic Anatomy.*—Meninges: Sections of the soft meninges in the region of the "pseudocyst" showed marked thickening of the membranes. No division between the pia and the arachnoid could be made out. The infiltrating neoplastic tissue brought about a fusion of the two membranes and removed all lines of separation. It was possible, however, to identify in some areas of the infiltrated meninges (fig. 4) several distinct zones, such as an outer pigment layer (*a*), then a zone which bore a strong resemblance to the histologic structure of a benign meningioma or fibroblastic endothelioma (*b*) and a third zone consisting of closely packed tumor cell nests assuming an alveolar arrangement of a rather characteristic appearance.

The latter showed the same uniform appearance and arrangement in every location, whether in the brain substance or in the meninges. The cells were

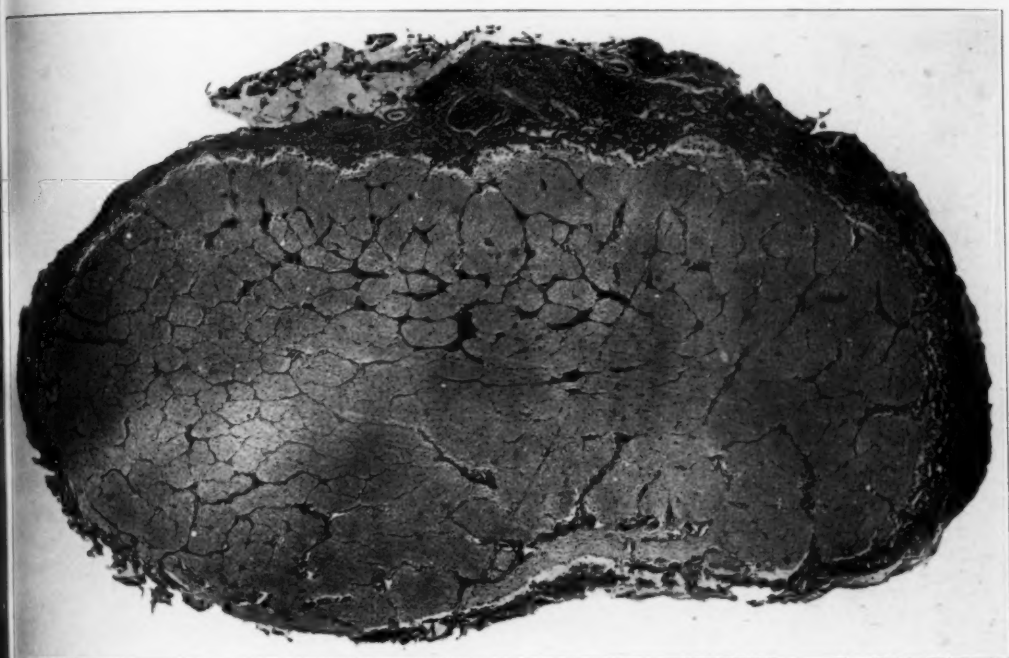


Fig. 7.—Optic nerve enveloped by the infiltrated leptomeninges.

epithelioid and somewhat irregular in outline, assuming pentagonal, or at times rounded, outlines. Their nuclei were large and rich in chromatin. The cytoplasm was fairly well outlined and most commonly free from pigment material. The dark appearance was due mainly to the deeply stained nuclei. These cells were usually found enveloping small blood vessels, assuming a radiating appearance and forming layers varying in number from three to eight.

The arrangement into three distinct zones did not hold true for the entire spread of the soft membranes, as there were regions in which narrow zones of pigment were stretched over rather wide areas of the alveolar structure, characteristic of the second layer. In this same zone, and in other areas, a palisade arrangement and whorl structures were conspicuous, while the more malignant

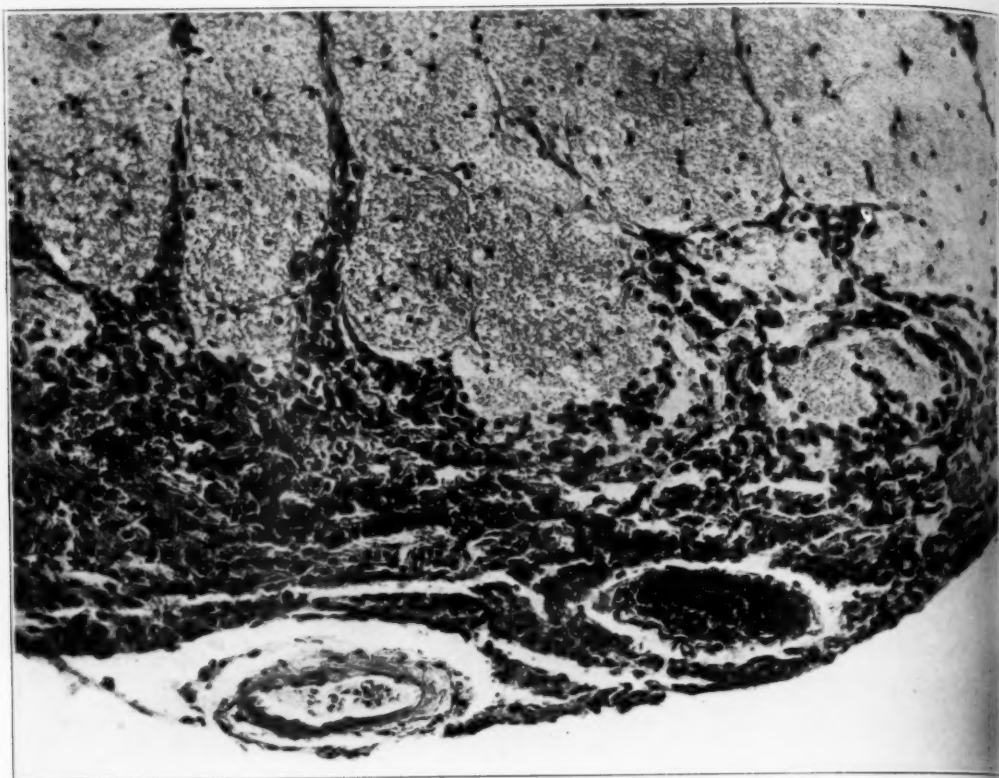


Fig. 8.—Optic nerve, showing the infiltrating cell and the extension of the invading neoplastic process along the trabeculae.

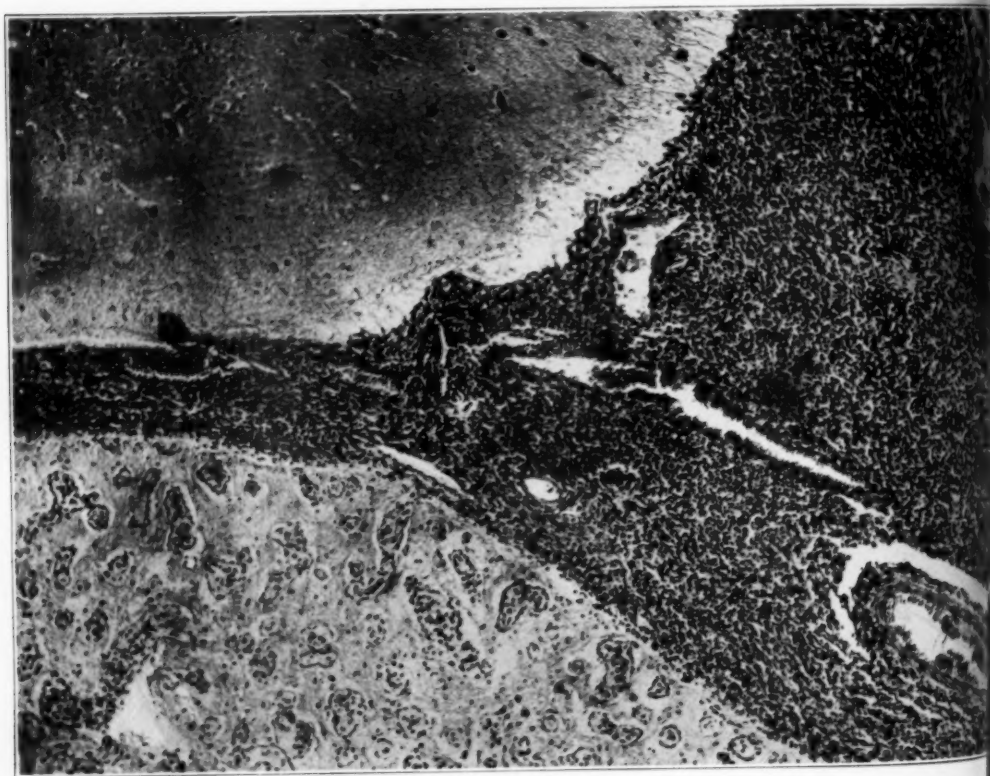


Fig. 9.—Leptomeninges over the surface of the brain. The infiltration here bears the character of a spindle cell sarcoma.

neoplastic islands found in the third zone were often absent or seen in small, almost negligible numbers.

In a third variation, seen particularly in the meninges covering the pons (fig. 6), the epithelial structures invaded the meninges in large masses. Here a connective tissue stroma was conspicuous and the pigment cells were diffused and irregularly distributed in patches throughout the entire thickness of the meninges.

Still another variation was seen about the cranial nerves. The optic nerve serves as a good illustration. Here (fig. 7), with a low magnification, the entire optic nerve was seen enveloped by a sheath of the pia-arachnoid, thickened and

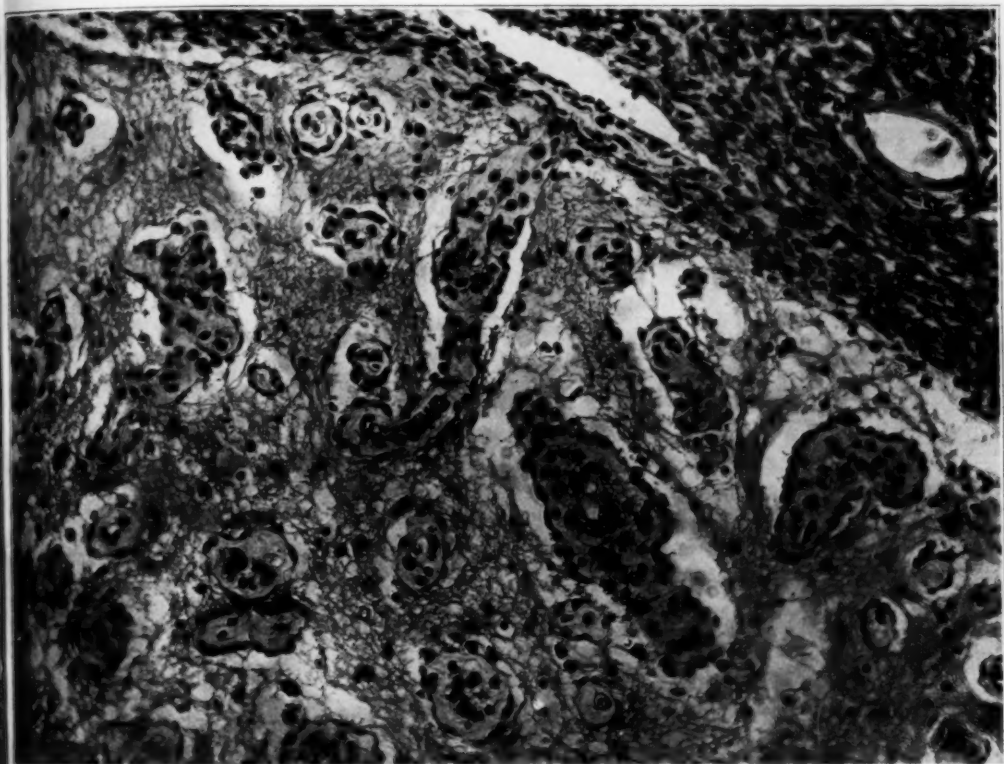


Fig. 10.—Leptomeninges over the surface of the brain, with the neoplastic process extending along the pial vessels into the brain substance.

infiltrated with extensions of the neoplastic meninges running through the entire nerve. Under a high magnification, it became obvious that little of the normal structure of the pia-arachnoid was left intact, that it was entirely displaced by neoplastic material (fig. 8). The cells were epithelial, containing here and there small groups of pigment-containing cells with the same type of cell extending along the trabeculae of the optic nerve.

Finally, the meninges covering the surface of the cerebral hemispheres showed another type of meningeal alteration. Here the pia-arachnoid was represented by a solid mass of somewhat elongated, occasionally rounded cells (fig. 9) and

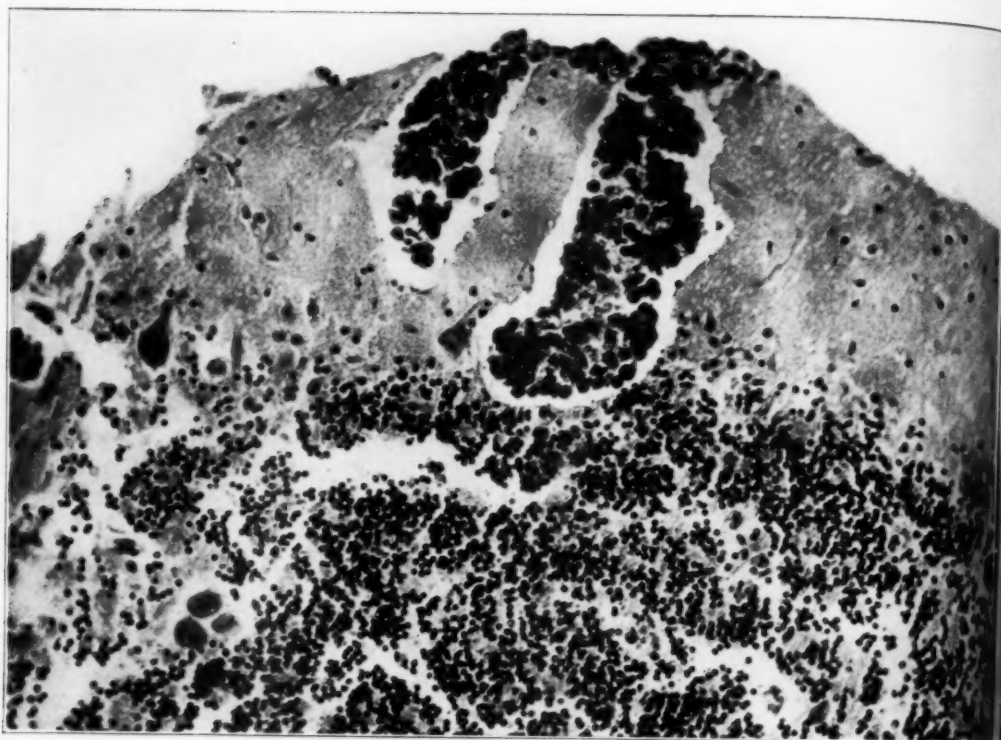


Fig. 11.—Cerebellar cortex, showing a small neoplastic extension.

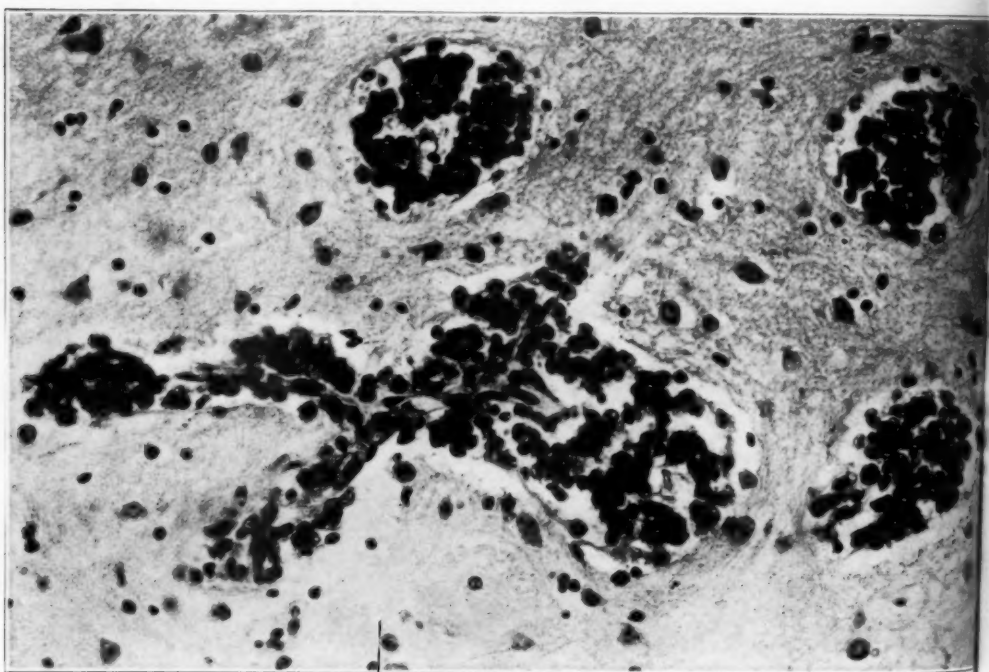


Fig. 12.—Pons, showing how infiltrating tumor cells follow the course of the blood vessels. pigment cells are seen in this area.

presented an appearance not unlike that of spindle cell sarcoma. The cells were rich in nuclear chromatin but were poor in cytoplasmic material. The infiltration of the meninges followed the extensions of the membrane into the fissures of the brain substance and along the penetrating pial vessels into the substance itself (fig. 10). The character of the cells along the pial vessels differed somewhat from that of the cells in the meninges covering the cerebral surface. In the former location they assumed a cuboidal character. Where these extensions into the brain substance were only slight, as in some of the cerebellar regions (fig. 11), the cell type reverted more to the one described in the third zone in the infiltrated meninges.

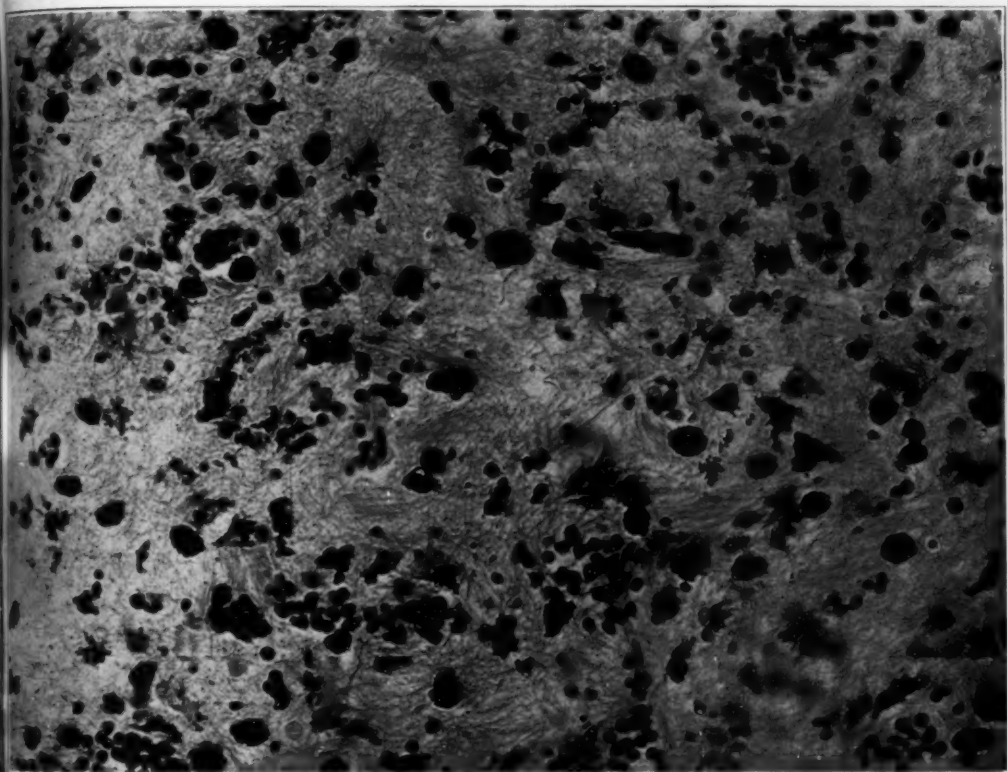


Fig. 13.—Pons, showing many infiltrating pigmented and nonpigmented tumor cells.

**Brain Substance:** The histologic picture showed several types of alteration; such variations could often be seen alongside one another. For example, in figure 12, which represents a section of the pons, there are aggregations of tumor cells of an epithelial character. They were arranged about the small blood vessels and followed the course of these vessels. In such locations, pigment material was strikingly sparse. At a short distance from this area (fig. 13) were numerous pigment-laden cells, true tumor cells, rounded or irregular in outline. Among them were glia cells, which apparently had phagocytosed pigment material and had assembled it in the periphery of the cell body. The glia cells were easily

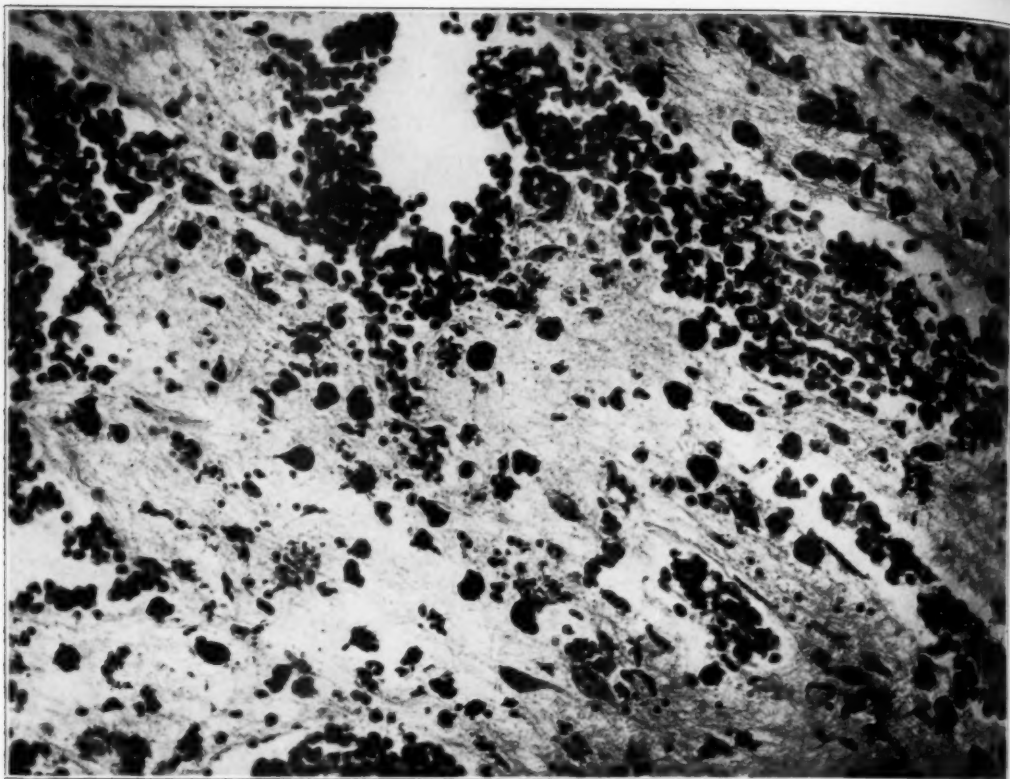


Fig. 14.—Pons: Areas of larger masses of nonpigmented tumor cells alternate with areas of less numerous pigmented cells.

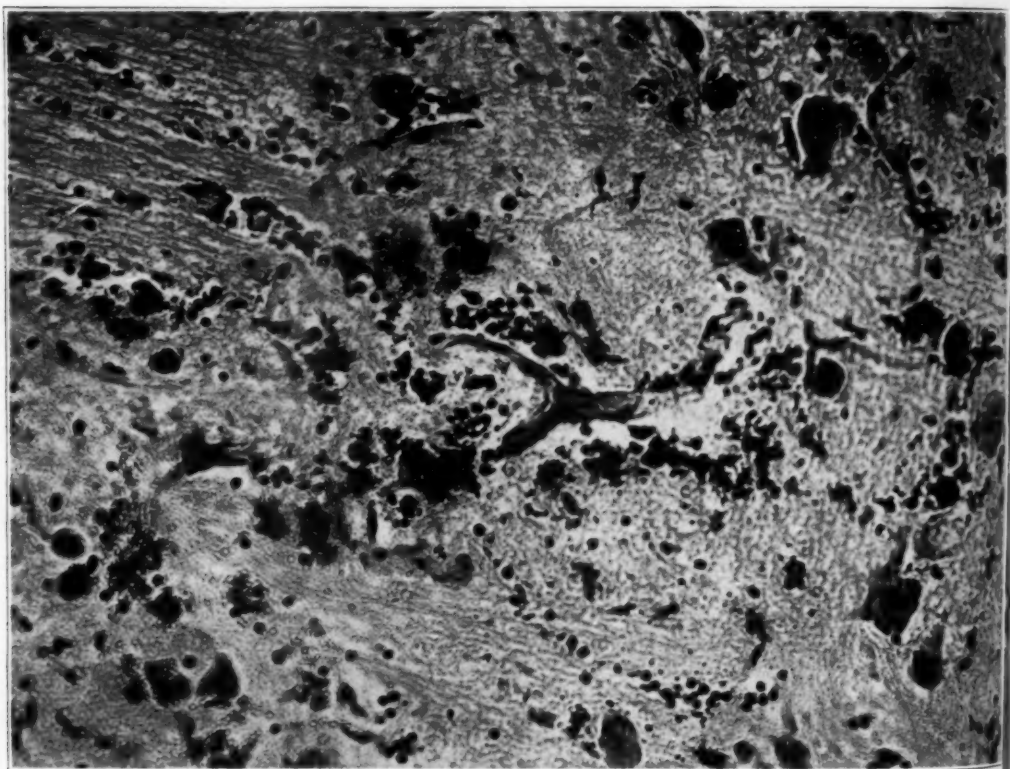


Fig. 15.—Blood vessels surrounded by pigment containing phagocytic elements. A few pigmented tumor cells are seen in the vicinity.

identified by their protoplasmic processes and by the arrangement of the pigment material at the periphery of the cell body; in the tumor cells, the finer structure was completely submerged under a thick covering of the pigment. Occasionally, pigment cells, with branching processes that had the outline of a chromatophore, were found in this area. An attempt to demonstrate microglia was defeated by the black pigment, which obscured the finer outline of these cells.

A transitional zone between the two areas described was often encountered; in it there were large aggregations of nonpigment tumor cells (fig. 14) alternating with massive aggregations of pigment cells. Here, again, glia cells with phagocytosed pigment were numerous, and areas were also noted, in parts remote from the tumor invasion, that were free from the nonpigmented type of tumor cells

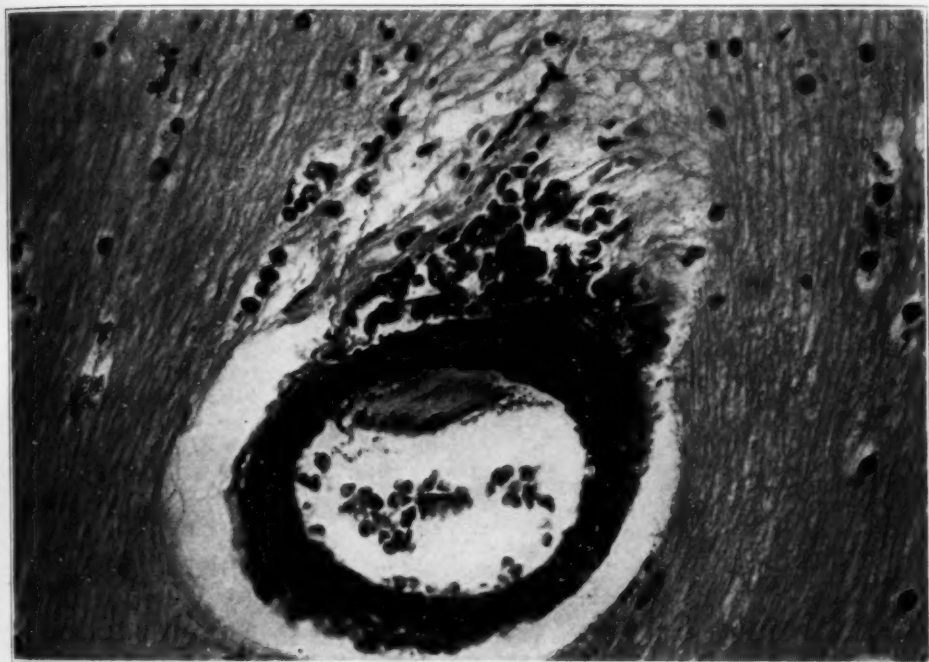


Fig. 16.—Blood vessel, with its wall stained by brown pigment and showing mild infiltration with pigment-containing cells.

and revealed only a few chromatophores and vessels surrounded by many gitter cells and glial elements filled with pigment (fig. 15). Occasionally, in zones entirely free from neoplastic invasion, isolated blood vessels with their walls colored by a brownish pigment were found surrounded by pigment-containing cells (fig. 16). The latter had the appearance more of phagocytic elements than of true pigment tumor cells. Here, also, were observed blood vessels that contained chromatophores in their lumina among the blood elements (fig. 17); this is difficult of interpretation, though microscopic study showed them to be similar to the cell structures in the tumor mass.

*Summary of Anatomic Observations.*—The main alteration was the infiltration of the meninges and brain substance by pigmented and non-

pigmented tumor cells. The cells were of several types: (1) The pigment-containing cell, which, though present in large numbers in the meninges, was more conspicuous in the invaded areas of the brain substance. In the former, it resembled somewhat the normal chromatophores. In the brain, it appeared as rounded masses of pigment with the cell structure totally obscured. (2) The epithelioid cell, which was irregularly round or pentagonal and provided with a fair amount of cytoplasm and a vesicular nucleus. It was striking to find that the pigment-containing cells occurred in areas in which the epithelioid cells

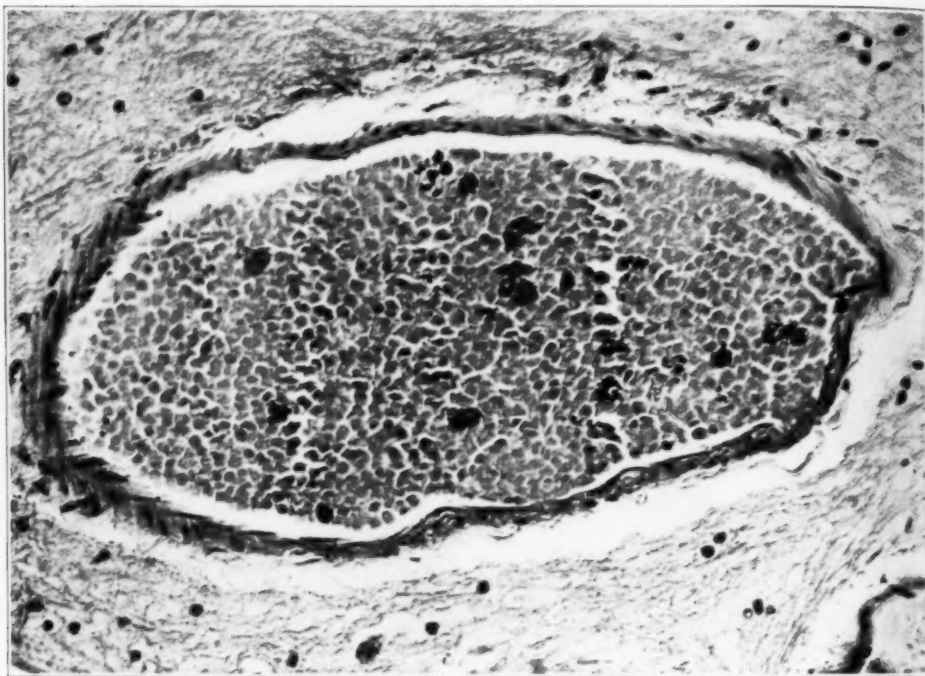


Fig. 17.—The lumen of this vessel shows, among numerous blood elements, typical chromatophores.

appeared in large numbers and vice versa. (3) The elongated, fusiform cell, which gave to some of the areas in which it appeared in large numbers the character of a spindle cell sarcoma.

In addition to these three main types of cells, there were numerous glial elements, including protoplasmic macroglia and microglia. The protoplasmic macroglia displayed small quantities of phagocytosed melanin pigment, while the microglia were so packed full of the dark pigment that their cell outlines became obscured. The pigment was

assumed to be of the character of melanin, since it failed to give an iron reaction with appropriate microchemical tests.

The cell arrangement showed a manifold organization: areas in which the neoplastic process assumed the character of a benign meningioma; areas in which it resembled a spindle cell sarcoma, and areas in which the alveolar, more malignant, character dominated the picture. Of interest, also, is the occurrence of marked vacuolization of the brain substance in regions in which the cerebral cortex was invaded by tumor elements. The subarachnoid space (fig. 10) was completely obliterated by the tumor tissue in these regions. It is not unlikely, as Hassin<sup>1</sup> has maintained, that this was caused by the inadequate drainage of tissue

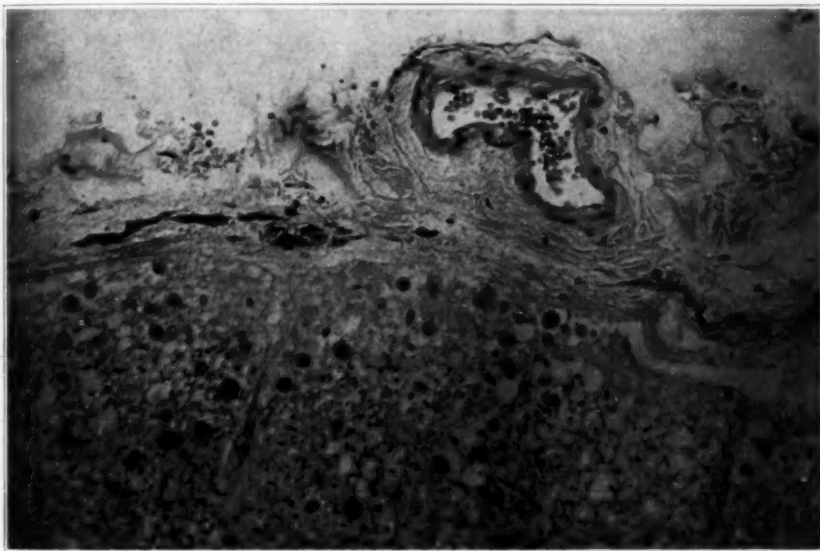


Fig. 18.—Chromatophores in the pia covering an adult medulla oblongata.

fluids by way of the Virchow-Robin spaces, which were blocked by the infiltrating tumor material.

The neoplastic process had its widest distribution in the meninges. It invaded the cerebral cortex and brain stem only secondarily and in a patchy fashion, and followed the cranial nerves along with the meningeal extension. The process was most conspicuous, because of the thickening and coloration of the meninges, at the base of the brain, particularly in the regions of the pontile and interpeduncular cisternae. Because of

1. Hassin, G. B.: Circumscribed Suppurative (Nontuberculous) Peripachymeningitis: A Histopathologic Study of a Case, *Arch. Neurol. & Psychiat.* **20**:110 (July) 1928.

the obliteration of the pontile and interpeduncular cisternae, the cerebrospinal fluid could not reach its distributing channels distal to these cisternae; hence the damming back of the fluid provoked the internal and external hydrocephalus. The latter was well demonstrated in the markedly distended cisterna magna, which acquired the character of a cyst.

## COMMENT

Clinically, there is little to be said, except that the only diagnostic hint was from the cerebrospinal fluid. The xanthochromia was probably, at least in part, due to pigment. A more careful search for cellular elements in that fluid might have disclosed the presence of melanophores.

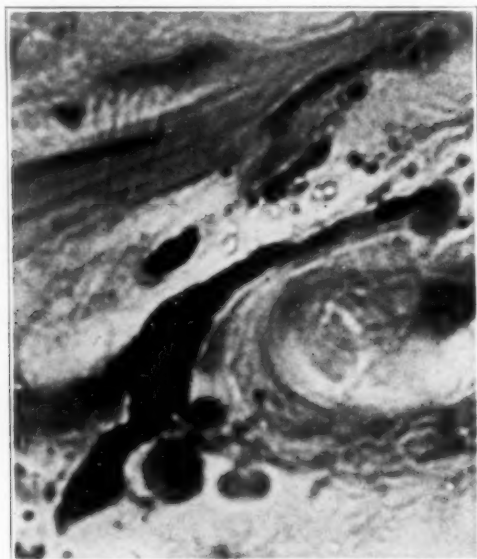


Fig. 19.—A chromatophore hugging a blood vessel.

The anatomic changes in our case are similar to those observed by Virchow<sup>2</sup> in a case described in 1859 as an instance of "primary melanosarcomatosis" of the arachnoid. In his case, as in ours, the outstanding features were: the absence of primary malignant tumor elsewhere in the body and the presence of a diffuse melanoblastic infiltration of the soft membranes. The pigmentation involved the arachnoid and the pia mater. It spread along the brain fissures, and filled the entire sheaths and fasciculi of the cranial nerves. In Virchow's case, the pigmentation formed also an almost unbroken chain of black flat

2. Virchow, R.: Pigment und diffuse Melanose der Arachnoides, *Virchows Arch. f. path. Anat.* **16**:180, 1859.

tumors surrounding an unaltered spinal cord and infiltrated spinal nerves and some of the spinal ganglia in a way similar to the cranial nerves; on the other hand, it did not invade the brain substance, as it did in our case.

Virchow regarded the widespread melanosis of the meninges as blastomatous and traced its derivation to the chromatophores, a normal constituent of the leptomeninges. These melanin-carrying cells had been described previously by Mohinke<sup>3</sup> and Valentin,<sup>4</sup> who were first to observe them in the leptomeninges of the normal adult brain. The existence of these cells in the pia covering the lower portion of the

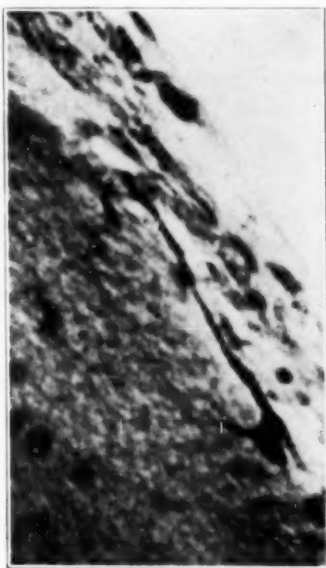


Fig. 20.—A chromatophore in the meninges of an infant, aged 2 months.

medulla and upper cervical segments of the spinal cord is now an established fact and can easily be verified by a diligent search for such cells in the leptomeninges of any normal adult brain. Their normal appearance is illustrated in the accompanying photomicrographs (figs. 18 and 19).

The claim was made that chromatophores do not appear in the human meninges before the age of 9 years. This apparently is not true, as we have been able repeatedly to find chromatophores in young

3. Mohinke, O.: Ueber Pigment in der Arachnoidea spinalis, Virchows Arch. f. path. Anat. **16**:1179, 1859.

4. Valentin, quoted by Virchow (footnote 2).

infants. In figure 20 is shown a chromatophore in an infant aged 2 months. We have found similar pigment-carrying cells in the meninges of a fetus of 5½ months.

During the seventy odd years following the report of Virchow's case, only a limited number of well studied cases have been described. Among them are those reported by Rokitsansky,<sup>5</sup> Sternberg,<sup>6</sup> Stoerck,<sup>7</sup> Grahl,<sup>8</sup> Herschberg,<sup>9</sup> Pick,<sup>10</sup> Minelli,<sup>11</sup> Boit,<sup>12</sup> Thorel,<sup>13</sup> Boesch,<sup>14</sup> Lindborn,<sup>15</sup> Lua,<sup>16</sup> Hesse,<sup>17</sup> Berlinger,<sup>18</sup> Esser,<sup>19</sup> Schoper,<sup>20</sup> Kiel,<sup>21</sup> Matzdorff,<sup>22</sup> Omodei-Zorini<sup>23</sup> and Baumbecker.<sup>24</sup>

5. Rokitsansky: Ein ausgezeichnete Fall von Pigment Mal mit ausgebreiteter Pigmentierung der inneren Hirn und Rückenmarkshäute, *Allg. Wien. med. Ztg.*, 1861, no. 15, p. 113.

6. Sternberg: *Verhandl. d. deutsch. path. Gessellsch.*, 1903, p. 167.

7. Stoerck, O.: Melanosarcomatosis Piae matris, *Wien. klin. Wchnschr.* **17**: 184, 1904.

8. Grahl, F.: Angeborener ausgedehnter Naevus pigmentosus in Verbindung mit Pigment-Flecken im Gehirn, *Beitr. z. path. Anat. u. z. allg. Path.* **39**:66, 1906.

9. Herschberg, A.: Chromatophoroma medullae spinalis: Ein Beitrag zur Kenntnis der primären Chromatophorome des Zentralnervensystems, *Virchows Arch. f. path. Anat.* **186**:229, 1906.

10. Pick, L.: Einige Rückenmarkstumoren, insbesondere ueber eine primäre melanotische Geschwülst, *Berl. klin. Wchnschr.* **43**:884, 1906.

11. Minelli, D. J.: Primärer melanotischer Gehirntumor, *Virchows Arch. f. path. Anat.* **183**:129, 1906.

12. Boit, Hans: Chromatophoroma (Ein Fall von Chromatophoroma durae matris spinalis, Beitrag zur Kenntnis des Chromatophoroma spinale), *Frankfurt. Ztschr. f. Path.* **1**:248, 1907.

13. Thorel, C. H.: Ein Fall von primärem melanotischem Sarkom der Rückenmarksmeningen, *München. med. Wchnschr.* **54**:725, 1907.

14. Boesch, G.: Ein Fall von primären Melanosarkom des Zentralnervensystems bei multipler Sklerose, *Zentralbl. f. inn. Med.* **33**:917, 1912.

15. Lindborn, O.: Ett fall af chromatoforoma durae matris spinalis, *Hygiea* **74**:198, 1912.

16. Lua: Ueber das primäre und das metastatische Melanosarcom des Zentralnervensystems, *Arch. f. Psychiat.* **53**:895, 1914.

17. Hesse, W.: Ein Fall von Melanose und primärer Chromatophormen der Meningen, *Beitr. z. path. Anat. u. z. allg. Path.* **71**:705, 1923.

18. Berlinger, W.: Ein Beitrag zur epithelialen Genese des Melanins: multiple Melanome der Haut mit Neurofibromatose der Hautnerven, melanotischer Tumor im Grosshirn, Gliom der Brücke, Sarkomatose der Meningen und hochgradiger angeborener Hydrozephalus bei einem ¾ jährigen Kinde, *Virchows Arch. f. path. Anat.* **219**:328, 1915.

19. Esser: Ueber eine seltene Rückenmarks Geschwulst (Chromatophoroms), *Deutsche Ztschr. f. Nervenhe.* **32**:118, 1907.

20. Schoper, K. J.: Ueber primäre Melanosarcomatose der Pia mater, *Frankfurt. Ztschr. f. Path.* **13**:77, 1913.

21. Kiel, E.: Diffuses Melanom der weichen Hirn und Rückenmarkshaut, *Centralbl. f. allg. Path. u. path. Anat.* **33**:393, 1922.

Of particular interest is the contribution of Omodei-Zorini, who attempted to analyze and reevaluate all of the cases recorded in the literature. He accepted the conception of Virchow as to the existence and derivation of primary melanotic tumors of the brain, and reemphasized it in a quotation from Lubarsch,<sup>25</sup> that primary melanocytoblastoma may develop only where melanin pigmented cells exist under normal conditions. However, he cautioned against an unrestricted use of the term "primary melanoblastosis" and demanded that the term be used only when there were no coexistent lesions which, by their capacity for metastasis, might excite doubt as to the primary character of the cerebral lesion. In drawing this conclusion, he was guided by the views of Lubarsch, who ruled that melanotic tumors of the brain or its meninges may be regarded as primary only if an exhaustive search fails to reveal any abnormal aggregation of melanotic cells elsewhere in the body, including the eyes and skin. The difficulty of ascertaining whether a pigmented mole or nevus is definitely and permanently benign, and the doubt that often surrounds the hidden potency for growth and metastasis of any pigment cell aggregation led Lubarsch to formulate his dogma that a melanotic tumor of any organ must not be considered as primary in the face of a coexistent pigmented mole or like structure. Using this rather rigorous rule, Omodei-Zorini, reviewing the various cases described as primary melanotic tumors of the central nervous system, concluded that a number of the recorded cases should be excluded from the group of primary melanocytoblastosis of the brain and of the meninges.

In a few of the instances he was fully justified, particularly when a previous operation for the removal of a pigmented tumor elsewhere in the body served as a good ground to deny a primary character to the lesion of the central nervous system. This holds true of the case reported by Dobbertin,<sup>26</sup> in which it was shown that a tumor of the eye had been removed ten years previously. In this case it might be suspected that the melanotic sarcoma of the eye was the primary focus, though the time that elapsed between the removal of the original growth and the metastasis was rather long. The case of Pol<sup>27</sup> also deserved

22. Matzdorff, P.: Eine diffuse Geschwulst der weichen Hirnhäute, etc., *Ztschr. f. d. ges. Neurol. u. Psychiat.* **86**:333, 1923.

23. Omodei-Zorini: Zur Kenntnis der primären Melanocytoblastoma der Pia mater, *Virchows Arch. f. path. Anat.* **250**:566, 1924.

24. Baumbecker: Zur Frage des primären Entstehens und der Wachstumsbedingungen des Melanoms im Gehirn, Frankfurt. *Ztschr. f. Path.* **37**:118, 1929.

25. Lubarsch: *Med. Klin.* **16**:195, 1920.

26. Dobbertin: Beitrag zur Kasuistik der Geschwülste: III. Melanosarcom des Kleinhirns und Rückenmarks, *Beitr. z. path. Anat. u. z. allg. Path.* **28**:52, 1900.

27. Pol, R.: Zur Kenntnis der Melanose und der melanotische Geschwülste im Zentralnervensystem, *Beitr. z. path. Anat. u. z. allg. Path.*, 1905, supp. 7, p. 737.

exclusion on the ground that the coexistent melanotic deposits in the viscera made the primary character of the process in the central nervous system doubtful. On the other hand, the refusal to accept into the group of primary melanoblastomas the cases of Rokitsky, Lua, Berlinger and Esser because of the existence of apparently benign pigmented moles in the skin, cannot be considered as final. However, it is his objection to the case of Grahl because of an extensive melanosis of the skin and of the non-neoplastic melanotic changes in the brain which leads us to believe that the dogma of Lubarsch is too rigid and must be either abandoned or modified; otherwise we shall be forced to the extreme of accepting the older views of Ribbert,<sup>28</sup> who at one time maintained that all melanotic tumors of the brain, cord and meninges are secondary growths with the primary focus either in the skin or in any other seat of normal pigment cell accumulations. We shall then be obliged to dismiss all cases so far recorded as primary melanotic tumors in the central nervous system, no matter how great an authority the investigator is, for the inability to demonstrate the presence of unusual accumulations of pigmented cells in the skin or other localities by careful gross or microscopic examinations does not preclude the existence of some hidden aggregation of such cells. It is obvious, then, that though a rigid dogma is unworkable, it is also defective in its basic principles.

There is a not infrequent concurrence of multiple tumor formations of divergent types, bearing no relationship to one another, in a single organism. A good illustration is tuberous sclerosis, a disease characterized by multiple disseminated neurospongioblastic foci, which is often accompanied by neoplastic lesions in other organs, such as myoma of the heart or fibroma of the kidney. In such conditions, one certainly must regard the blastomatous process in the brain as unrelated to the changes in other organs, except in the sense that the same cause is operative in the malformations in two distinct organs.

In the same manner, extensive maldevelopment in the organization and distribution of pigment in several parts of the body may occur synchronously, without one area being the seat of metastatic formation of the other. Moreover, why can there not be an exclusive pigment malformation in one part of the body with a similar but more extensive spread of pigment deposit elsewhere without the latter assuming the character of a secondary growth?

In this connection, the case of Grahl gains significance; there was an intensive melanosis of the skin and a similar melanosis of the

28. Ribbert, H.: Ueber das Melanosarkom, Beitr. z. path. Anat. u. z. allg. Path. **21**:471, 1897.

meninges. It was said that in both localities the pigmentation did not acquire the character of a neoplastic process. This precludes any suggestion that the pigmentation of the meninges is a metastatic and not a primary process. The case serves as a good illustration of the concurrence of two independent sites of melanosis both of which are primary and one of which is in the meninges.

#### CONCLUSIONS

Primary melanoblastosis of the central nervous system does occur. The primary character of melanoblastosis of the central nervous system is not impeached by the presence of dormant collections of pigmented cells in the form of quiescent pigmented moles or nevi elsewhere in the body.

## THE HYPOTHALAMUS

A SEGMENTAL STRUCTURE AND A REGULATOR OF GLANDULAR  
ACTIVITY AND METABOLISM \*

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NEW YORK

Since the two major subjects in the title deal with the question of segmental and suprasegmental structures, on the one hand, and the control of glands on the other, some definitions are in order to clear the way for the presentation of the proofs which can be offered to substantiate the thesis of the paper.

By segmentation is meant a process of division of the body and its controlling nervous system from head to tail-end in such a manner that, in primitive animals at least, each segment is identical to each of the others. In the process of evolution changes have occurred in many segments, particularly in those of the cephalic and caudal ends. The intermediary segments in some instances are also modified. However, in spite of this, the segments of the body are recognized with comparative ease, and so far as their neural elements are concerned, each has an afferent system, a connecting system and an efferent system. In the process of evolution, all or part of either the afferent or efferent system may disappear.

The suprasegmental part of the nervous system develops from only that part of the neural tube which lies dorsal to the sulcus limitans, a line which divides its dorsal receptor from its ventral effector parts. The suprasegmental portion of the nervous system includes the cerebellum, the colliculi, certain portions of the septum, the ventral and dorsal thalamus including the geniculate nuclei, the paleostriata and neostriata and the cerebral cortex.

Glands may be classified as those of external secretion, those of internal secretion, and those having both internal and external secretion. Certain glands now of internal secretion only—such as the pituitary and thyroid—were primitively of external secretion, emptying into the cephalic end of the alimentary canal. The lung is also an outgrowth

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\* Submitted for publication, Dec. 12, 1930.

\* Read by title at the Fifty-Sixth Annual Meeting of the American Neurological Association, June 10, 1930.

of the primitive alimentary canal. The glands shown in figure 1 are those of the alimentary canal.<sup>1</sup>

For the thesis of this paper it is also necessary to recall the cephalic and caudal locations of the segmental nervous system in control of assimilation and emptying in an animal with a cephalocaudal axis. Though to my knowledge the proof is lacking, it seems probable that animals with a cephalocaudal axis have developed from circular animals in which no such axis exists. The appearance of the power to move from one place to another is accompanied by the development of the head and tail end of the animal, the former of which, as Sherrington pointed out, contains the guiding segments and the distance receptors. The head end of the animal is for assimilation, while the tail end of the animal is for emptying, as Cannon has emphasized. There is a tendency for those parts of the nervous system that have to do with the control of the organs concerned with assimilation to be drawn by cephalotaxis toward the head end, while those parts of the nervous system that have to do with the control of emptying are drawn by caudotaxis to the tail end. It is interesting in this connection that the vagus nerve supplies the gastro-intestinal tract up to the end of the small intestine, thus implying that it supplies that part of the intestine that is concerned with assimilation. The large intestine is normally concerned only with absorption of water. The vagus nerve supplies most of the digestive glands (fig. 1). The large intestine and rectum are supplied by the pelvic nerve (Gaskell).

There is much evidence that the hypothalamus has all of the characteristics of a segment and none of the characteristics of the suprasegmental parts of the central nervous system. It is now well known that the pituitary gland is connected to the hypothalamus by the tractus hypothalamicohypophyseus of Greving. Beyond a supply by the thoracic sympathetic system, it has no demonstrated visceral nervous system control except this tract; that is, no autonomic supply. On the other hand, no suprasegmental part of the central nervous system gives off efferents to a gland.

Furthermore, in animals below man the nervus terminalis terminates in this region of the nervous system. This, the first cranial nerve, contains receptor fibers as well as effector visceral fibers belonging to the sympathetic system and supplying branches of the anterior cerebral

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1. There is evidence that the secretion of the pituitary gland drains into the cerebrospinal fluid, which makes this gland one of external secretion in a certain sense. It is also interesting to note that the primitive cerebrospinal canal connects by the neurenteric canal to the primitive digestive tube. Evidence that the parathyroid glands were of the excretory type in lower forms has not been found.

artery. Suprasegmental parts of the central nervous system do not have peripheral nerves.

It may be seen that the hypothalamus lies below and behind the sulcus limitans (fig. 2). The suprasegmental parts of the central nervous system are always above, not below, the sulcus limitans. This same relation obtains in all vertebrates. The work of Tilney and Shultze, and Kingsbury is of interest in this connection, as they disagree as to the precise anterior termination of the sulcus limitans. However, there is much evidence that this anterior termination in the region of the infundibulum lies anterior to it.

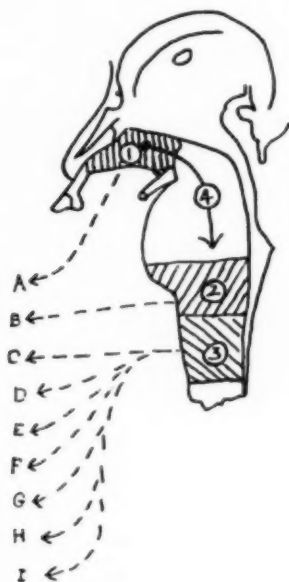


Fig. 1.—*A* indicates the pituitary gland; *B*, the salivary; *C*, the thyroid; *D*, the parathyroid; *E*, the lungs; *F*, the gastric glands; *G*, the hepatic; *H*, the pancreatic, and *I*, the intestinal. The segments of the central nervous system controlling glands concerned with metabolism are as follows: (1) hypothalamic region; (2) region containing salivary nuclei (Kohnstamm); (3) region containing vagus nuclei; (4) path from the hypothalamus to the brain stem.

Fiber paths from the hypothalamus to the tegmental region of the brain stem, in which lie nuclei of the visceral and branchial nervous systems, have already been demonstrated in all classes of vertebrates (Kappers). From the point of view of this paper, these are considered intersegmental paths controlling, at least, the pontomedullary segments shown as 2 and 3 in figure 1, and so the glands supplied by them. The existence of these paths may account in part for the large size of the

hypothalamus, all of which it seems unlikely could be required for pituitary control.

Regarding the matter from the point of view of general metabolic processes, it is known that the pituitary gland plays an important part in regulating sleep, temperature, respiration, blood pressure and pulse rate. In addition, the fundamental metabolic processes carried out through the metabolism of water, sugar, fats, proteins and salts are also influenced by this gland. Through its control of the pituitary gland, the hypothalamus regulates these activities.

Finally, the metabolic rate itself is so controlled, as the following quotations indicate:

The metabolic rate in pituitary disease apparently varies according to the stage of the disease and the amount of functioning gland substance. Reports indicate that the metabolic rate may be accelerated during the earlier stages of acromegaly, but that it is commonly reduced during the latter phases, the reduced metabolic

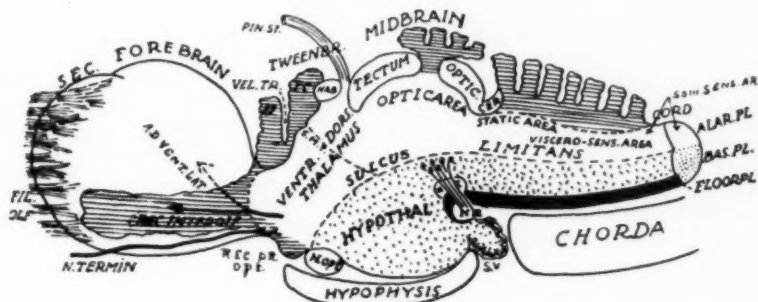


Fig. 2.—Schematic representation of the chief subdivisions of the brain in a primitive fish. *N. termin.* indicates nervus terminalis (failing in the lamprey, but present in all other fishes); *rec. pr. opt.*, recessus praeopticus; *s. v.*, saccus vasculosus (failing in the lamprey, but present in all other fishes); *pin. st.*, pineal stalk; *p. p.*, paraphysis; *p. c.*, parencephalon; *n. i.*, nucleus interpeduncularis (Kappers).

rate occurring at the period when the patients gain flesh. In diabetes insipidus, a disease of the posterior lobe of the pituitary, the basal metabolism is normal or slightly increased (up to plus 30 per cent—Snell et al.). In two cases of Fröhlich's syndrome the same observers found the basal metabolism normal. My own experience is in accord with these results. Aub believes that the metabolic effects of pituitary disease are brought about through the medium of the thyroid gland. Such a view is supported by McKinlay's work which seems to show a synergism between pituitary and thyroid glands (King).

Benedict and Homans performed hypophysectomy in dogs and studied the total metabolism through the carbon dioxide elimination. The results of this operation were:

1. Tendency to gain in body weight
2. Slightly lowered body temperature
3. Marked fall in pulse rate which became slower a few days after operation and maintained a low level

4. Fall in respiratory rate comparable to the fall in pulse
5. Marked diminution in total metabolism, as determined through the elimination of carbon dioxide. The fall in metabolism per unit of weight was even more striking, owing to the deposit of fat
6. Retardation of growth and sexual development in young animals

Such evidence combined with the clinical aspect of pituitary disturbances which will be discussed later, indicate that the hypophysis has a profound effect on metabolism. The question arises in connection with the interpretation of pituitary effects whether they are due to the immediate effect of this gland on metabolism or whether they may be produced by the pituitary acting through the thyroid gland. The results of hypophysectomy are strikingly similar to the results of thyroid insufficiency, and Aub feels that the hypophysis probably affects the metabolism through the medium of the thyroid. It is also of interest that Boothby has noted the common occurrence of the signs of thyroid disease in patients with pituitary disorders (King).

The close relation of the hypothalamus to the pituitary is tersely described by Cushing in the following:

Probably, therefore, the effects are the same whether produced by (1) an injury to the hypothalamic centers, (2) a "block" of the nervous impulses with obstruction of the secretory products in the posterior lobe, or (3) a partial hypophysectomy with actual removal of the lobe. In other words, a break in the mechanism of posterior-lobe secretion from nerve center to gland, produced by any agency, tends to upset the normal water balance and to cause an hypophysial polyuria; and conversely, the administration of posterior-lobe extract serves to check the experimental polyuria thus produced whenever the break in the mechanism may have occurred.

As the pituitary gland was originally a gland of external secretion that emptied its secretions into the alimentary canal and has developed into a gland of internal secretion, and as it regulates all metabolic processes rather than any single metabolic process, it would appear (fig. 1) that the most cephalic end of the segmental nervous system which controls the pituitary is an extremely primitive and altered segment of the central nervous system regulating metabolism in general. The remaining glands having fewer functions are regulated by the less cephalad segments of the central nervous system. The hypothalamus thus regarded is the guiding segment of that part of the segmental central nervous system which is concerned with visceral functions.

## THE HANDEDNESS AND EYEDNESS OF SPEEDERS AND OF RECKLESS DRIVERS \*

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SAN FRANCISCO

In carrying out the experimental work of which this paper gives a brief account, the main object was to ascertain by simple tests what percentages of the various sinistral types were to be found, respectively, among two classes of persons, those arrested for violation of section 113 and those arrested for violation of section 121 of the California "State Vehicle Act."

These sections read as follows:

Section 113.—Any person driving a vehicle on the public highways of this state shall drive the same at a careful and prudent speed not greater than is reasonable and proper, having due regard to the traffic surface and width of the highway, and no person shall drive any vehicle upon a public highway at such a speed as to endanger the life, limb or property of any person.

Section 121.—Any person who knowingly and wilfully drives any vehicle upon a public highway, either without due caution and circumspection or in such a manner as to endanger the life, limb or property of any person shall be guilty of reckless driving.

### MATERIAL AND TECHNIC

All of my experimental data were secured in department 10 of the Municipal Court of the city of San Francisco, in which court all traffic cases are tried. In each instance the necessary observations were made in the chambers of the presiding judge. Here, as circumstances permitted, I was enabled to examine persons whose cases had been disposed of in the adjoining court room at the average rate of 9 a day. Eight of my subjects were women; all of the rest were men. These persons were tested, without selection, in the order in which they presented themselves. Of the 500 persons thus examined, 354 were charged with exceeding the speed limit, 121 had been arrested under the charge of reckless driving, and 25 had committed the offense of driving while intoxicated. In this paper, however, I shall deal only with the first and second groups.

The question as to the handedness of any given person was determined by having him execute the movement of throwing a ball, while that as to his eyedness was decided by means of a pointing test. Details as to the technic may be dispensed with in this paper, as I have described these tests at length in another paper.<sup>1</sup>

\* Submitted for publication, Aug. 25, 1930.

1. Quinan, C.: The Principal Sinistral Types, *Arch. Neurol. & Psychiat.* 24:35 (July) 1930.

The statistical data used in the preparation of this report were compiled from records kept on file in the office of the San Francisco city prison.

I shall describe first the general results secured by means of the visuomanual tests and afterward take up in detail some other observations that concern, respectively, the group of speeders and the group of reckless drivers.

#### EXPERIMENTAL RESULTS

*Relative Percentages of Dextrals and Sinistrals Noted Among Speeders and Reckless Drivers.*—The general outcome of the survey on sinistrality is shown graphically in chart 1. It will be noted that this

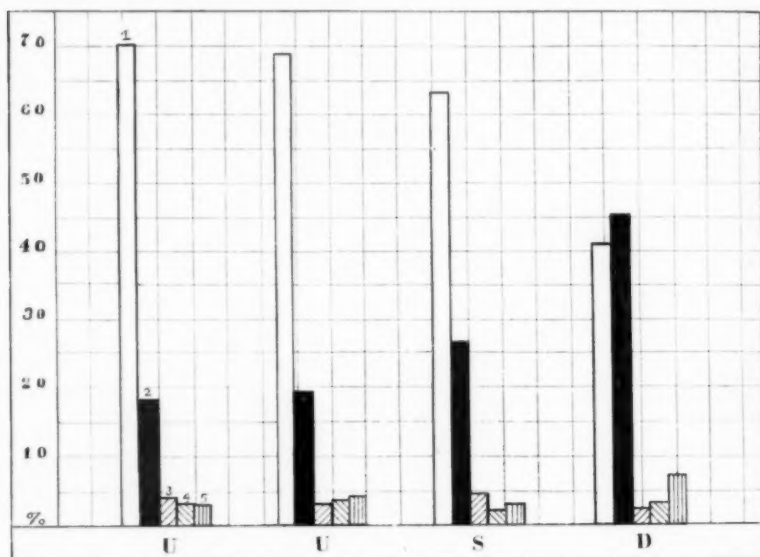


Chart 1.—Percentages of the principal visuomanual types found among university students, speeders and reckless drivers. The first series of 1,000 was tested in March, 1929; the second series of 1,331, in August, 1929. *U* represents university students; *S*, 354 speeders; *D*, 121 reckless drivers; 1, symmetrical dextrals (RR), right-handed and right-eyed; 2, asymmetrical or cross-wired dextrals (RL), right-handed and left-eyed; 3, symmetrical sinistrals (LL), left-handed and left-eyed; 4, asymmetrical or cross-wired sinistrals (LR), left-handed and right-eyed, and 5, ambilaterals—neither eye dominant.

chart also exhibits two sets of values secured by the same method of examination from undergraduate students in the University of California. The results noted at the university have been introduced for the sake of comparison.

On referring to chart 1, it can be seen at a glance that the percentages (RL) for right-handed and left-eyed persons present the most striking

variations, and that the irregularities to be noted in this respect concern only the two groups of subjects studied at the traffic court. As a matter of fact, the earlier studies, carried out on different occasions with university students, had shown that the RL value varied but slightly, since the first series of tests had given an end-result of 18.5 and the second, an end-result of 19.7 per cent. On the other hand, 26.8 per cent of the speeders were found to be right-handed and left-eyed persons, while 45.4 per cent of the reckless drivers were persons of that type; indeed, as may be seen in chart 1, in this latter group the RL sinistrals actually outnumbered the dextrals. In other words, if, as seems fair, 19 per cent is accepted as the basic RL value, it follows that the values obtained among speeders and reckless drivers were, respectively, 7.8 and 26.4 per cent above normal. Therefore, though limited in amount, the foregoing evidence seems to show that persons of the RL type, for some unknown reason, are especially prone to drive their cars "without due caution and circumspection." I suspect that this tendency may be related in some way to a factor to which I have called attention in the paper previously referred to, namely, that in many instances, such persons exhibit evidences suggestive of what, for want of a better term, may be called constitutional instability.

As regards frankly left-handed persons, the results obtained were of little value, because, necessarily, the number of such persons tested was small. In the two university groups the collective values noted with respect to the two left-handed types of sinistrality—left-handed and left-eyed (LL) plus left-handed and right-eyed (LR)—in the first series of tests had been 7.6 per cent, in the second, 6.9 per cent. The respective figures obtained among speeders and among reckless drivers were 6.7 and 5.7 per cent. However, as far as they go, these experimental observations seem to leave the left-handed drivers with a clean score.

Concerning the remaining, ambilateral group (A-L), a group made up of persons in whom it was difficult or impossible to determine which eye was dominant, the results obtained in the two university groups and among the speeders were nearly the same, that is, approximately 3.5 per cent; in the group of reckless drivers this value was 7.4 per cent.

As a fact that seems worthy of remark, I may add that the figure representative of total sinistrality (45.4 plus 5.7) in the group of reckless drivers amounted to 51.1 per cent.

*Relation Between the Age Data and the Speed Data.*—The average miles per hour rating at the moment of arrest in the cases of 354 speeders (chart 2) was 41.4 miles. In this particular, the difference between the respective speed averages of dextral and sinistral drivers was so slight as to be negligible—it was only a small fraction of a mile. The following relation existed between the age data for the drivers and

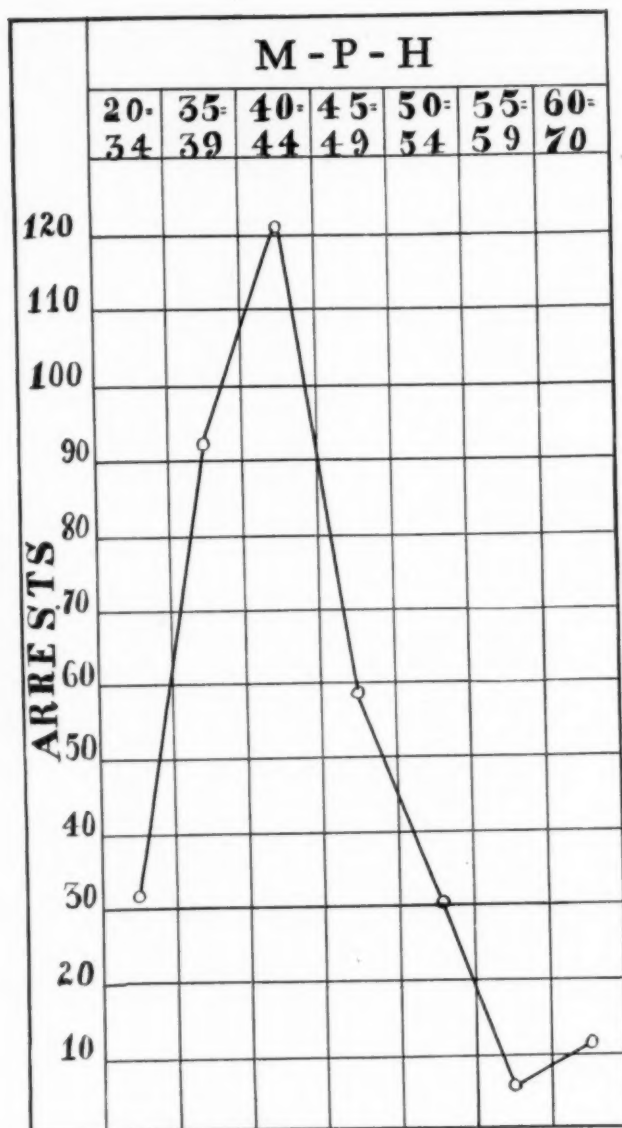


Chart 2.—Miles per hour ratings of 354 speeders.

the mileage data: The data for the age of those who drove up to 49 miles per hour remains constant, since, at all speed levels up to that point, it was found that 62 per cent of the drivers were under 30 years of age; on the other hand, of those who drove from 50 to 59 miles per hour 71 per cent were under 30 years of age, while the average age of 12 drivers arrested for traveling at rates above 60 miles per hour was 19.4 years. Therefore in practically every instance of excessive speeding, it is safe to assume that the driver is under 20 years of age. The average age found for the entire group of 354 speeders was 27.5 years.

It should be understood that the "tags" issued to reckless drivers seldom bear speed notations. The reason why such tags bear no mileage data is that reckless drivers are usually taken into custody because of some traffic accident in which property is damaged or in which one or more persons are injured or killed.

*Classification of Reckless Drivers.*—While, from a psychologic point of view, some reckless drivers are much like the average type of speeder,

TABLE 1.—*One Thousand Speeders and One Thousand Reckless Drivers Compared with Respect to Their Ages*

Age Distribution													Totals	Mean
Subjects	14 to 19	20 to 24	25 to 29	30 to 34	35 to 39	40 to 44	45 to 49	50 to 54	55 to 59	60 to 64	65 to 69			
Speeders.....	141	308	200	146	102	43	33	17	8	2	0	1,000	27.8	
Reckless drivers.	94	239	221	166	95	80	46	36	14	8	1	1,000	30.3	

of those whom I examined, more than half differed decidedly from that average. Of such drivers there were two distinct groups. The larger one of these groups was made up of highly excitable persons who in a nervous sense were obviously ill balanced and unstable. Many of them were men of the RL type. The other group consisted of peculiarly stolid, unresponsive persons. It was noticeable that subjects of this kind executed the simple visuomanual tests in a manner that was both hesitant and incomplete. For example, instead of carrying out a vigorous throwing movement, as requested, frequently a member of this group would merely pick up the ball in a cautious, gingerly way and then, having raised it slightly, let it fall on the examiner's table where it would perhaps bounce feebly a few times before it fell off. From the way in which these men fumbled with the ball, the idea suggested itself that their limited capabilities in the direction of muscle coordination might possibly be explained in terms of some time reaction factor; but, however that may be, one could foresee, as regards any one of them, that in the presence of a serious traffic emergency he would probably lose his head and be responsible for a crash. All of these drivers were middle-aged dextrals.

## SPECIAL DATA RELATIVE TO SPEEDERS AND RECKLESS DRIVERS

*Average Ages.*—Having noticed while the experiments were in progress that these two classes of offenders seemed to differ from one another definitely as regards the age factor, I was not surprised to find, on comparing the experimental results, that this difference amounted to a little more than two years, and that the reckless drivers constituted the older group. However, since I had made comparatively few observations, and the question as to an age difference seemed important, I collected some additional statistical evidence on this point (table 1). As the data agreed in every respect with the figures previously noted, showing the same peculiarities as to the age groupings and yielding the same general average, there seems to be no doubt that as a class reckless drivers are about  $2\frac{1}{2}$  years older than speeders.

TABLE 2.—*Number of Speeders and Reckless Drivers Arrested in the City of San Francisco for a Period of Eight Months, by Respective Monthly Totals*

Date	Speeders	Reckless Drivers	Total Arrests	Reckless Drivers, per Cent
November, 1929.....	436	103	539	19.1
December, 1929.....	378	127	505	25.1
January, 1930.....	403	137	540	25.3
February, 1930.....	540	112	652	17.1
March, 1930.....	536	125	661	18.9
April, 1930.....	473	95	568	16.7
May, 1930.....	685	129	814	15.8
June, 1930.....	545	102	647	15.7
Totals.....	3,986	930	4,916	19.2

*Relative Numbers.*—As had been the case in the study of the age question, my statistical data on this subject were carefully compiled in the office of the San Francisco city prison from official records on file there. This information was sought with two objects in view: (1) by comparing the respective figures as to total monthly arrests to ascertain if possible whether a numerical relation of any sort can be made out between the two classes of offenders under consideration; (2) to determine whether during periods in which the traffic laws are enforced more rigidly than usual, and consequently there is great activity on the part of traffic officers, the number of persons arrested for reckless driving shows a corresponding increase. Such pertinent data as I was able to obtain are embodied in table 2 and figure 3.

Table 2 shows, by monthly totals for a period of eight months, the number of persons arrested for speeding as well as for reckless driving, together with figures that show the percentages of such persons who were said to be reckless drivers. It will be noted that the percentage figures relative to the latter dangerous class of offenders were com-

paratively high in the two winter months of December and January, whereas they were considerably lower in November and in the period of five months from February to June. Particularly striking was the fact that, although the figures as to the total number of persons arrested per month remained approximately the same during November, December and January, arrests made under the charge of reckless driving were relatively high only during the two winter months. This discrepancy was puzzling, and I was unable to account for it at the time. Further study of the facts, however, brought to light a possible explanation.

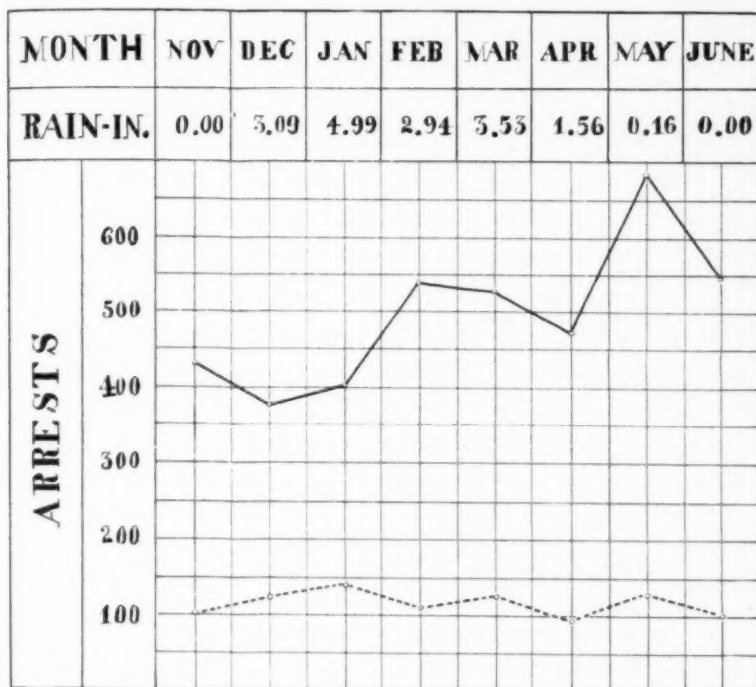


Chart 3.—The numbers of speeders and reckless drivers arrested in the city of San Francisco during a period of eight months by respective monthly totals. The solid line represents speeders; the broken line, reckless drivers.

When the foregoing arrest data had been plotted on curve paper (chart 3), they at once assumed an entirely different aspect; for then it became apparent that the figures representative of the total number of arrests made per month under the charge of reckless driving, though a bit high during December and January, varied but little during the remaining six months. Moreover, this graphic presentation of the facts seemed to show clearly: (1) that no relation exists between the number of persons arrested for speeding and the number of persons appre-

hended as reckless drivers, and (2) that the number of reckless drivers arrested during special "drives" against offenders of the traffic law was no greater than the number of such persons arrested at other times. Here, then, were definite answers to the two questions previously raised.

It may now be asked: Why were so many reckless drivers arrested last winter during the months of December and January? In order to find an answer to this question it is necessary to bear in mind two facts: (1) every year, immediately after Christmas, many new and inexperienced car owners make their appearance on the streets; (2) the average condition of the traffic surface at that time of the year is often such as somewhat to increase the difficulties attendant on the operation of motor vehicles. This, at any rate, was the case in San Francisco last winter, for on a number of occasions the city was visited by torrential rains, and its streets, rendered slippery by such periods of wet weather, presented unusual hazards to drivers. I believe that this unfortunate combination of circumstances—unskilled operators and wet streets—was responsible for the fact that a comparatively large number of so-called "reckless drivers" were arrested during those two months.

Though worthy of remark in passing, the small seasonal increase just spoken of is evidently unimportant, because the figures in table 2 show that during a period of eight months the number of arrests made per month under the charge of reckless driving varied within comparatively narrow limits; as a matter of fact, they show that the traffic court handled cases of that description at an average rate of about 116 per month.

With the data at my disposal, I can add only a rough conjecture concerning the incidence of reckless driving as expressed in terms of car ownership statistics. But since, according to official records, 153,503 motor vehicles of all kinds were registered in 1929 as belonging to residents of San Francisco, it appears that approximately 1.3 per thousand of the local motoring public are arrested each month as reckless drivers. However, if allowance is made for the fact that in some instances the defendant had been arrested more than once for that offense, while in other instances there was little evidence to support so serious a charge, the figure given can probably be scaled down to a value considerably below 1 per thousand.

#### CONCLUSIONS

1. Of 2,331 university students, 19 per cent were RL sinistrals. Among 354 speeders and 121 reckless drivers the RL percentages were 26.8 and 45.4, respectively.
2. Six and seven tenths per cent of the speeders and 5.7 per cent of the reckless drivers were left-handed men—LL plus LR.

3. The average miles per hour rating of 354 speeders was 41.4. This value was constant for both dextrals and sinistrals.

4. The age data referable to 1,000 speeders and 1,000 reckless drivers gave respective mean values of 27.8 and 30.3 years.

5. There seems to be no relation between age and speed for all levels up to 50 miles per hour; beyond that point, however, the average age value falls, and twelve drivers with ratings of from 60 to 70 miles per hour had a mean age of 19.4 years.

6. In San Francisco for eight months the arrests for reckless driving averaged 116 per month; expressed in terms of car ownership statistics, this gives a rate of about 1.3 per thousand.

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## PUPILLARY DISTURBANCES IN SCHIZOPHRENIC NEGROES \*

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Pupillary disturbances in catatonic patients were first described by A. Westphal.<sup>1</sup> He observed that the pupils show "seemingly irregular changes in their reaction to light, ranging from a prompt reaction to absolute rigidity, frequently with sluggishness, but always with changes in form." He also found that the pupillary reaction in convergence was often preserved. Loewenstein<sup>2</sup> showed that the so-called Redlich phenomenon of the pupils also can often be observed in catatonic patients. Redlich<sup>3</sup> was the first to describe the fact that in epileptic persons strong muscular exertion sometimes provokes pupillary rigidity, but he was also able to demonstrate that similar muscular exertion in other patients also diminishes, and even abolishes, the pupillary reaction to light. He interpreted the phenomenon as the effect of the muscular strain. Loewenstein considered the emotional factor connected with the muscular exertion as the basic cause of the pupillary phenomenon. Shortly after Westphal's discovery, E. Meyer<sup>4</sup> was able to provoke a diminution and an abolition of pupillary reactions to light by means of

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1. Westphal, A.: Ueber ein im katatonischen Stupor beobachtetes Pupillenphänomen, *Deutsche med. Wchnschr.* **33**:1080, 1907; Ueber Pupillenphänomene bei Katatonie, Hysterie, etc., *Monatschr. f. Psychiat. u. Neurol.* **47**:187, 1921; Ueber Pupillen bei Encephalitis epidemica, *Ztschr. f. d. ges. Neurol. u. Psychiat.* **68**:226, 1921; Zur Frage des von mir beschriebenen Pupillenphänomens bei Post-encephalitis (Spasmus mobilis), *Deutsche med. Wchnschr.* **51**:2101 (Dec.) 1925.

2. Loewenstein, O.: Ueber die Variationsbreite des Lichtreflexes und der Psychoreflexe der Pupillen, *Arch f. Psychiat.* **82**:285, 1927; Ueber die Natur der sogenannten Pupillenunruhe, *Monatschr. f. Psychiat. u. Neurol.* **66**:126 (Oct.) 1927; Ueber die sogenannte paradoxe Lichtreaktion, *ibid.* **66**:148 (Oct.) 1927.

3. Redlich, E.: Ueber ein eigenartiges Pupillenphänomen, *Deutsche med. Wchnschr.* **34**:313, 1908; Zur Charakteristik des von mir beschriebenen Pupillenphänomens, *Monatschr. f. Psychiat. u. Neurol.* **49**:1, 1921.

4. Meyer, E.: Die körperlichen Erscheinungen bei Dementia praecox, *Ztschr. f. Psychiat. u. psychisch-gericht. Med.*, vol. 66, 1909.

pressure against the iliac point. Muscular exertion and iliac pressure often provoke mydriasis and even a change in the shape of the pupil. According to Westphal, the pupillary changes in catatonic patients are generally combined with mydriasis. Because of their inconstancy, Kehrer<sup>5</sup> called these pupillary phenomena "spasmus mobilis." In some cases, however, the phenomena persist for a considerable time, and Westphal described cases in which pupillary rigidity was the regular state for considerable periods, being interrupted only occasionally for transient periods by good pupillary reactions. According to Koester,<sup>6</sup> the frequency of these changes in catatonic persons, if the pupils are frequently examined over a long period, is found to be about 34 per cent. Other authors, however, have not found such a high percentage of changes. Reichmann,<sup>7</sup> for instance, found marked pupillary changes in 8 of 215 cases examined, but 6 more were added when Meyer's method was employed. Menninger<sup>8</sup> found marked disturbances in the pupillary reaction to light in 25 per cent of 400 patients examined over an extensive period of time.

According to the wide experience of one of us (P. S.) in the Viennese psychiatric clinic, even the smaller percentages quoted by Menninger and Reichmann are much too high if one considers only the patients available for observation in a psychiatric clinic. Only two cases of marked pupillary changes in catatonic persons were seen in the course of several years at the Viennese psychiatric clinic; a report of one of these cases was published by H. Hartmann.<sup>9</sup> In such a department the patients cannot, of course, be observed for any great length of time, and it is possible that the difference in frequency may be partly due to the difference between acute and chronic cases. Long observation of a single case, however, offers a better opportunity for recording the phenomenon, since the pupillary disturbances are sometimes present for only a short time and then disappear.

We examined the patients of the psychopathic department of Bellevue Hospital systematically for pupillary changes. We found that in the course of three months there were only two cases of marked pupillary changes, in the sense already described, among all of the white schizophrenic patients admitted. Among the colored schizophrenic

5. Kehrer, F.: Zur Pathologie der Pupillen, *Ztschr. f. d. ges. Neurol. u. Psychiat.* **81**:345, 1923.

6. Koester: Ueber die Häufigkeit des Vorkommens des Spasmus mobilis, *Arch. f. Psychiat.* **81**:601, 1927.

7. Reichmann, Frieda: Ueber Pupillenstörungen bei Dementia praecox, *Arch. f. Psychiat.* **53**:302, 1913-1914.

8. Menninger, W. C.: Eye Signs in Schizophrenia, *Arch. Neurol. & Psychiat.* **20**:186 (July) 1928.

9. Hartmann, H.: Pupils in Catatonia, *Wien. klin. Wchnschr.* **37**:1013 (Oct. 2) 1924.

patients, however, we found a number of cases with marked disturbance of the pupillary reactions, although the number of Negroes is less than 10 per cent of the number of white patients. Among twelve schizophrenic colored women there were six with distinct changes in the pupillary reactions, and of twelve schizophrenic men there were five with similar pupillary disturbances. We considered as positive only such cases in which the sluggishness and incompleteness of the reaction was marked. In all of these cases the signs of Meyer and of Redlich were positive to a greater or less degree. From a methodologic point of view, it must be noted that the negroid pupil is more difficult to study than that of the white person because of the dark color of the iris. The patient's resistiveness to the examination also makes it still more difficult at times. Perseverance and great care at repeated examinations is necessary. Another difficulty is presented in the fact that the psychiatric diagnosis of psychosis in Negroes is in many respects not always easy. There is a primitive type of motility with tendencies to rhythmic movements. The emotions of colored people are also decidedly more difficult to understand. Religious content and ecstatic experiences are common even in healthy Negroes, and superstition of all kinds is widespread among them. Many symptoms that are of use in the diagnosis of schizophrenia in a white person are useless and even misleading in making a similar diagnosis in Negroes. Furthermore, syphilis is a common disease among colored people. The blood and spinal fluid were examined in most of our patients, but we know that there are certainly pupillary changes in syphilitic cases in which tests of the blood and spinal fluid give completely negative results. It may be said by some that the catatonic pupillary disturbance is so different from the syphilitic pupillary change that a differential diagnosis can easily be made. As we shall discuss later, we cannot approve of such a statement, for if the syphilitic pupillary change is not complete, the disturbances already described are common also in the pupils of syphilitic persons. We shall return to this problem later. In spite of all these difficulties, however, one can be sure that in mental conditions in Negroes that belong to the schizophrenic and, especially, to the catatonic type, pupillary changes of the character described by Westphal are common.

We may emphasize that among the schizophrenic cases with pupillary changes that we have observed, catatonic symptoms prevailed. In the negative cases, paranoid symptoms were predominant. Thus far in the paraphrenic cases, we have not seen pupillary disturbances.

The pupillary changes in our cases may be described as follows: Usually the pupils are mid-wide or somewhat larger. We have not seen pupils that were extremely dilated. In one of the cases to be reported, there was marked narrowness of the pupils, but such cases are the exception. The reaction to light is generally better than the reaction in

accommodation, but in some of our cases even the latter reaction was absent. Changes in the width of the pupils are common. The pupils usually remained regular in shape in our patients, and even in those that manifested irregularities the deviation was comparatively small. In all of our patients, the pupils retained reaction to pain and dilated when pain was provoked. The impairment of the pupillary reaction to light varied from sluggishness to complete rigidity. From our material we have taken only the cases that showed at least marked sluggishness. Iliac pressure and active muscular exertion, with the exception of one case reported, either had no effect on the width of the pupils or made them somewhat wider. In one case the pupils narrowed. We did not find a positive Redlich or Meyer phenomenon without changes in the spontaneous reaction of the pupils to light. We found that the Meyer phenomenon is never present without the Redlich phenomenon and vice versa. In rare cases, active muscular exertion or iliac pressure may improve the pupillary reactions, but even in such cases, with the same method on other occasions, we found a definite impairment of the pupillary reactions. Frequently the pupillary reaction to light may change in the course of one series of examinations. One must only be careful not to flash the light too frequently because even in a healthy person this method may lead to impairment of the pupillary reaction. In many of our cases the impairment was observed to be essentially the same on the two sides, but frequently there was a marked difference in the reaction of the two pupils. In some cases, an examination on the following day revealed a complete reversal of the reactions in the left and the right sides. We shall present abstracts of some of the more interesting cases.

#### REPORT OF CASES

CASE 1.—J. J., a man, aged 22, a typical American Negro, whose family history revealed a trend of nervousness and emotional instability, was the fourth of nine children. He roamed a great deal and loved to remain by himself. He had previously been arrested for disorderly conduct. He was admitted to Bellevue Hospital after stealing a car and subsequently colliding with a street car. In the hospital he showed sudden outbursts during which he attacked other patients. He reported that for many years he had heard the voice of his mother and that spells were cast over him. On June 23, 1930, he said: "I'm saving everybody in here. I'm King Bee. The officer put his cap on my head and made me king, and I saw it through the screen. He made me captain. I came out of the White House this morning. I will certainly go East this morning." He hit two patients in the eye on this morning. In explanation, he stated that they waved their feet and made his feet go to sleep, and that they also laughed at him. He spoke of leprosy in the room. He showed an unmoved facial expression. The pupillary reactions were prompt.

On June 28, the pupils were almost rigid, especially the right one. They were not more than mid-wide. For the past few days he had complained that people laughed and spit at him. He had not, however, again been aggressive. He was

quiet and more seclusive at this time, and lay near the window. Half an hour later, the pupils were markedly dilated and reacted poorly.

*Comment.*—We report this case because it shows particularly how, in a patient with apparently normal pupillary reactions, a sudden change or even a disappearance of the reactions can occur.

CASE 2.—M. T., a man, aged 36, an American Negro, with not very dark skin, was brought to the psychopathic department of Bellevue Hospital on May 1, 1930, after having been found on the street saluting in a military manner and shouting that he was a delegate for the Elks. He said that the lights were giving him signals. According to his brother, he was a heavy drinker, but the brother could say nothing concerning the onset of the present illness. The patient said that the people at "the building" started clawing at him for using three fingers, and that one of them asked him why he used them. Then, he said, "she broadcasted" and told everybody about his using those fingers, and that they called him bad names. He said that the people who worked in his building wanted to get him out of his position; they had picked on him for the past few months, and had watched him in the building and on the street. "I began to learn a little science about dreams. I'm always going to places in my sleep and have different things shown to me. I'm not a scientist, but I can understand such true things. I'm always guided by my mind." He was silly, rambling, talkative and disconnected.

The pupils were small, irregular in outline and practically fixed to light. The spinal fluid was clear, under normal pressure and showed no globulin reaction, no increase in cells, a negative colloidal gold curve and a negative Wassermann reaction. The Wassermann reaction of the blood was negative.

On May 2, he was pseudocataleptic, moved his mouth in a fishlike manner and said: "I'm directing you. That's the other street and this is the cross street. I'm standing on the square. I teach wisdom here. Some people abuse me and kick me around." The reaction of the pupils to light was incomplete on both sides, but the convergence reaction was much better. A little later, the pupils were wider and reacted almost normally to light. When the patient squeezed the physician's hands, however, the pupils became very narrow and absolutely fixed to light. Iliac pressure had the same effect. In the course of the next few days there was no change in the pupillary reactions, and the patient became somewhat more resistive.

*Comment.*—This case is noteworthy because of the narrowness of the pupils. When they were small they became rigid; when they were wider they reacted well. It is remarkable that active and passive pressure provoked narrowness of the pupils and an absence of the reactions. Clinically, the case is one of typical schizophrenia with some catatonic symptoms.

CASE 3.—A. D., a woman, aged 25, a British West Indian Negress, was admitted to the hospital on May 13, 1930, after having been picked up in the street in a disturbed condition, overtalkative and expressing religious ideas. The day after admission, she said: "I think I been under the spell since I began to love a man. Then he put his family watching me. The Blessed Mother said to me, 'If you talk too much the people in St. Mark's Church will get you. They

will set a trap for you.'” The patient said that she heard the voices while the mission was going on. The pupils were dilated and reacted well to light. On the following day, she said that the Blessed Mother had brought her to America to save America. The pupillary reactions were changeable in both eyes and sometimes almost absent. Active muscular exertion as well as passive abdominal pressure provoked almost absolute rigidity of the pupils to light, and they simultaneously became somewhat wider. The face had a vacant expression. In the course of the next three days, the mental condition cleared up; the patient became quiet and cooperative, and the pupillary reactions became normal. Bodily, she was of a dysplastic type. The blood and spinal fluid were normal in every respect.

*Comment.*—In this case there was an acute paranoid condition, which disappeared within a short time. The clinical classification remains unclear. We report the case in order to illustrate how transient reactions (either schizophrenic or schizoid) may be connected with pupillary changes. In the next case, the diagnosis of schizophrenia is clearcut.

CASE 4.—T. J., a woman, aged 22, a typical American Negress, was admitted to the hospital on June 13, 1930, with a statement from her husband that she had lost her way a year previously and had seen and talked with devils. She had recovered from this attack shortly afterward. For a week prior to the present admission, she had been depressed and uncommunicative, smiling in a silly manner to herself. The day before admission, she had prayed a great deal. She remained uncommunicative, but obeyed orders and requests. She gave up passively assumed postures slowly and sat stiffly, but was not negativistic. She would suddenly clap her hands.

The pupillary reactions were prompt even on muscular exertion. On the day of admission to the hospital the patient showed marked catalepsy, but obeyed orders well. She showed a marked reaction to turning of the head. The pupils were wide, but did not react well to light, the left being almost stiff. The reactions were the same on abdominal pressure and changed frequently in character. On June 17, the right pupil was almost rigid, while the left reacted somewhat better; the reactions were still changeable, however. The patient continued to be cataleptic. On June 18, the pupils reacted promptly, but the mental symptoms had not changed appreciably.

*Comment.*—We report this schizophrenic case to illustrate the fact that changes in the mental picture do not run parallel with changes in pupillary reactions. The case also shows that the right and left pupils do not always react in the same manner.

CASE 5.—A. G., a woman, aged 31, a very dark-skinned British West Indian Negress, was first admitted to the hospital on April 28, 1930, five days post partum, because she had become excited in the obstetric ward of the Lincoln Hospital and expressed visual hallucinations of two babies. The physical condition was essentially normal; the patient rested quietly, expressed no hallucinations or delusions, and was taken home by her husband after three days. Four weeks later, on May 28, 1930, she was readmitted to the hospital with a statement that she had become depressed, thought that she was going to die that night and had become very religious. She moaned continuously and said: “Please, don’t take my life, doctor. I’m innocent of it all now. The Lord look down. The

people on the street said I belong to the State. I hear them saying I'm a bum and a dirty dog and you got me here to die like a dirty dog. You all said I went with Dr. T. I thought I had a black and a white baby, but I never went with no white man." She was excited and resistive to examination.

The pupils were mid-wide, the right a little irregular in outline, and both were stiff to light. Two days later, she was still moaning, overtalkative, apprehensive and shouting: "I will never do it again." The pupils were still almost rigid. A week later, she was much quieter. The right pupil was practically fixed and irregular in shape. The spinal fluid was found normal in every respect. Subsequently, the patient became more and more dull and stiff in her emotional life. The depression practically disappeared and was replaced by stupor, so that the diagnosis of schizophrenia was more evident. The pupillary disturbance had suggested this diagnosis at a time when the clinical picture alone was more distinctly that of a depression. This was a case of schizophrenia combined with pupillary changes developing post partum.

In order to increase the extent of our statistical material, we examined eleven colored men and fifteen colored women (all schizophrenic) in the Manhattan State Hospital. Dr. I. J. Furman, medical superintendent of the hospital, aided us in this study. Of the eleven men there were four, and among the fifteen women there were twelve who manifested pupillary disturbances. These patients were examined only once or twice. Most of them had been in the state hospital for over two years. These patients as well as those in the Bellevue Hospital included both American and West Indian Negroes. There appeared to be no difference between the two groups, although our material may be too small for any definite conclusion.

#### COMMENT

There arises, of course, the question whether the pupil in Negroes does not show a greater tendency than that in white persons to the phenomena of Westphal, Meyer and Redlich. Our investigations among Negroes give no basis to this opinion. We found but one psychopathic Negress with pupillary changes of the type under consideration, but similar phenomena have also been observed in white persons. Westphal found pupillary changes in a case of traumatic neurosis whenever he discussed the question of withdrawing the compensation. We have not thus far seen similar changes in manic-depressive Negroes.

This leads directly to the question whether the pupillary disturbances described by Westphal and by us are characteristic of schizophrenia. Westphal said that they are not. He observed the phenomenon in a case of traumatic neurosis, pointed to the possibility of similar changes occurring in some cases of hysteria, and described identical states in cases of epidemic encephalitis. Nielsen and Stegman<sup>10</sup> observed a nor-

10. Nielsen, J. M., and Stegman, L. N.: A Case of Nonsyphilitic Pupillary Inaction, *Arch. Neurol. & Psychiat.* **16**:597 (Nov.) 1926.

mal person with signs of vegetative imbalance who manifested pupillary rigidity from time to time. Kehrer, too, did not think that these changes are specific evidence of catatonia. We found similar changes in every pupil having a slightly impaired reaction or in which a previous damage to the pupillary reaction could be proved. It is convincing in this respect that in patients of any kind who have received scopolamine hydrobromide, hyoscine, homatropine or morphine, either hypodermically or as eye drops, the restitution phase shows phenomena that are identical with the pupillary changes described in our schizophrenic patients. The reaction in these phases is changeable and sometimes disappears completely when the patient exerts active pressure or is pressed at the iliac point. This is equally as true of the narrow pupil following administration of opium or morphine as when atropine or hyoscine is used. This experience makes it all the more necessary to make sure, in the diagnosis of pupillary changes in catatonic patients, that they have not received one of these drugs. Alcohol may have a similar effect on the pupils. Among alcoholic patients with delirium and hallucinosis we found many in whom similar phenomena were present, although absolute rigidity was rare. In alcoholic hallucinosis, the emotional state of the patient appears to have something to do with the pupillary disturbances. One patient with epilepsy and strong emotional disturbance manifested a state of marked muscular tension when he left his bed. The pupils became rigid, although at other times they reacted well. The stiffening of the muscles coincided, in this case at least, with the pupillary changes. It may be mentioned also that in the pupils of syphilitic persons having incomplete or only slightly impaired reaction, the reaction to light may be found changeable and subject to influence in the same manner as in catatonic patients. The experience of Westphal respecting the pupils in persons with epidemic encephalitis is identical with our own.

The material cited might lead to an impression that the so-called catatonic pupillary disturbances are due to a slight organic or toxic damage of the pupillary apparatus. Such an interpretation would not, however, explain the fact that similar changes can be found in purely psychogenic cases. There must be pupils which constitutionally react in a different manner to emotions and to the conditions of the Meyer and Redlich phenomena. In this respect, it is noteworthy that the sister of the patient described by Hartmann was examined by one of us (P. S.) at a time when she presented a typical neurasthenic picture. There was no sign of a syphilitic infection and the Wassermann reaction of the blood was negative. She showed rather well marked changes of the pupillary reactions, but they were not as distinct as those of her sister. The mother at that time developed hypochondriac delusions of a paranoid type, but her pupillary reactions were prompt. This

observation proves the importance of a constitutional factor for the genesis of catatonic pupillary changes. The sister of one of our Negro patients also had defective pupillary reactions. We do not doubt that investigations of a greater number of cases will show that pupillary disturbances among catatonic Negroes are more common than they are among white persons, but the constitutional-racial element alone cannot explain the difference. It is probable that the constitutional factor is of a somatic rather than of a psychic type. Loewenstein was able to show by graphic methods that there are different constitutional types in respect to the pupillary reaction to light among normal persons, and that some of these types are more closely allied to the catatonic reactions. Redlich remarked that his phenomenon can also be observed in normal persons to a slight degree.

In addition to the constitutional factor, however, there must be an additional psychic or toxic factor. We are inclined to believe that a psychic element alone is hardly sufficient. Westphal and Hartmann noted that pupillary changes frequently do not run parallel with changes in the psychic picture; our experience corroborates this. If there were only a psychic factor, one would have difficulty in explaining the individual differences in two pupils. A psychic factor, nevertheless, plays some part. Frequently, one observes that the first iliac pressure or the first muscular effort has a greater influence on the reaction of the pupils than do later trials (see also Loewenstein<sup>11</sup>). Not infrequently also, one sees that the first reaction to light is less than later reactions. It is especially the fact that almost identical psychic pictures sometimes are, and on other occasions are not, accompanied by pupillary disturbances (this also occurs in white persons) that hinder us from placing the psychic factor in the foreground of our interpretation.<sup>12</sup> We conclude, therefore, that the disturbances in the pupillary mechanisms described here are based on: (1) a constitutional factor, and (2) the organic state of the pupillary apparatus, due either to a lesion or to a toxic influence; this may include any change in the muscular state or in the state of the sympathetic nervous system; (3) the psychic factor. In the psychogenic cases, factors 1 and 3 operate together. In catatonic cases, factors 1 and 2 are probably of greater importance than factor 3. Factors 2 and 3 are effective in the cases of syphilis or of intoxication with alcohol, scopolamine hydrobromide, etc.

11. Loewenstein, O. (footnote 2, first reference).

12. We have not discussed the genesis of the Meyer and Redlich phenomena. That the psychic factor plays some part in both seems certain. But we are inclined to believe, with Redlich, that the muscular exertion as such has some specific effect. The Meyer phenomenon involves the functioning of the sympathetic or the parasympathetic nervous system.

Westphal was of the opinion that the phenomena described by him and by us are due to striopallidal lesions. He pointed especially to the pupillary changes in postencephalitis. We do not think that the same interpretation is admissible for all cases of spasmus mobilis of the pupils. We believe that a great deal of study will be necessary in order to find out which pupillary apparatus is affected in a given case. A definite proof of a striopallidal influence on the pupils has not yet been presented.

#### SUMMARY

In this paper, we report pupillary changes in catatonia as being much more frequent in Negroes than in white persons. A constitutional factor appears to be essentially responsible, and it is probable that this factor concerns the pupillary apparatus as such. Pupillary changes of the so-called catatonic type may be observed in any pupil which is affected by a toxic or an organic lesion of a slight degree. We found them particularly in cases of intoxication with alcohol, scopolamine hydrobromide and morphine. The phenomena are due to a coincidence of constitutional, psychic and anatomic-toxic factors.

## Clinical Notes

### ACUTE ASCENDING PARALYSIS (LANDRY'S PARALYSIS) WITH ACUTE IDIOPATHIC HEMATOPORPHYRIA\*

CYRIL COURVILLE, M.D., AND V. R. MASON, M.D., LOS ANGELES

In 1859, Landry described an acute disease of the nervous system of which the chief symptom was an ascending paralysis of rapid development that ended, as a rule, in death from asphyxia. The motor paralysis was of lower motor neuron type with loss of tendon reflexes. Sensory changes were minimal or absent. The sphincters were usually not disturbed. No gross or microscopic alterations of the nervous system could be demonstrated by the methods of study available at the time.

For many years there was a tendency to force into this group every instance of acute ascending paralysis, and as a result classification became much confused. This tendency was especially apparent in the reports of purely clinical studies on patients whose nervous systems had not been adequately examined after death. As larger series of case reports became available for study, it seemed probable that acute ascending paralysis, with more or less variation of the clinical symptoms from those described by Landry, represented a type of reaction of the nervous system during the course of various infections and intoxications.

The introduction of modern methods of examination of the nervous system greatly clarified the subject. Examples of the syndrome without gross or microscopic alterations of the nervous system were reported less frequently, and it became apparent that even in the most acute instances of the disease a demonstrable lesion of the nervous system was to be expected. The severity and topography of the lesions proved to be variable. In some instances the peripheral nerves alone were damaged, while in others the gray matter of the cord or the anterior horn cells presented the greater alteration. In some the lesions seemed purely degenerative, while in other cases the process was inflammatory. Gradually, therefore, Landry's paralysis has come to be regarded as a clinical syndrome without a uniform etiologic or histologic basis.

We recently observed a patient with acute, idiopathic hematoporphyria, in whom the disease terminated fatally following the development of an acute ascending paralysis of short duration.

#### REPORT OF CASE

*History.*—A white man, aged 36, began to complain of nervousness, sleeplessness and pains in the arms and legs during September, 1929. The pains increased in intensity and were not relieved by acetylsalicylic acid or a derivative of barbitol. On October 3, he had severe abdominal cramps which radiated into the thighs. He vomited frequently. There was slight fever. The leukocyte count was 16,000. An exploratory laparotomy was performed, but no abnormality was found except a dilated colon. Severe cramplike pains in the abdomen radiating into the chest

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\* From the Medical Service of the Los Angeles County General Hospital.

and thighs persisted, and morphine was required for relief. A barium enema was given on the thirteenth postoperative day. A greatly dilated loop of large bowel was present under the left leaf of the diaphragm. The patient was very ill. At times he was apathetic and at other times delirious. There were apparently hallucinations of sight and hearing. Careful examinations of the motor and sensory functions could not be made. Great muscular weakness of the legs and arms was present. The tendon reflexes of the legs and then of the arms became sluggish and finally disappeared. On November 1, dysphagia and dysarthria were noticed. He drooled saliva. Articulation and deglutition became impossible. Complete flaccid paralysis of the arms and legs was present. Coma, followed by incontinence, ensued, and the patient died on November 10. Except for a slight leukocytosis, the blood was normal. The cerebrospinal fluid was normal. The Wassermann reactions of the serum and the spinal fluid were negative.

The urine, examined on Oct. 16, 1929, was deep red and contained a dark brown sediment. Urobilin was present. On extraction by Garrod's methods, a large amount of hematoporphyrin was obtained. As the disease progressed, the color of the urine gradually approached normal, but hematoporphyrin was constantly present. The blood urea, nonprotein nitrogen and sugar content were normal.

*Autopsy.*—The body was well developed, but only fairly well nourished. The skin was normal, except for some brownish pigmentation of the face. There was a well healed abdominal incision. The thyroid contained a cystic adenoma. The lungs were free in the pleural cavities. They were somewhat congested, and on section showed areas of frank purulent bronchitis. The heart was normal. The abdominal viscera were essentially normal. On microscopic examination after appropriate staining, the liver showed slight cloudy swelling and much amorphous iron-free and iron-containing pigment.

*Nervous System.*—The brain, spinal cord and sections of the large trunks of the brachial plexus were removed at necropsy and hardened in 10 per cent formaldehyde. Grossly, the meninges, brain, spinal cord and peripheral nerves presented no abnormalities. In the coronal sections of the brain a few small, smooth-walled, fluid-filled cavities were observed, evidently due to postmortem infection with the gas bacillus.

Blocks were taken from the various lobes and parts of the brain, spinal cord and the large trunks of the brachial plexus for microscopic sections. The following stains and methods were employed: hematoxylin and eosin, Nile blue sulphate and scharlach r for fat, van Gieson's and Perdrau's methods for connective tissue, Mallory's phosphotungstic acid hematoxylin and aniline blue methods for glia and connective tissue, silver carbonate and gold sublimate methods for neuroglia, Bielschowsky-Pilch's method for Nissl's substance, Bielschowsky's method for neurofibrils and a modified Wright's method for myelin sheaths. The osmic acid method of Marchi was also used on blocks of peripheral nerves.

The only demonstrable change in the constituents of the brain, as demonstrated by the various methods, was minor chromatolytic alterations in the ganglion cells of the cortex, which may have been due to postmortem change or to a minor terminal toxic state rather than to the disease itself. No pigment was found in any of the sections.

The elements of the spinal cord were unchanged, except for the anterior horn cells, which had undergone a variable degree of chromatolysis. The tigroid sub-

stance in some cells was confined to a ring of granules about the periphery of the cytoplasm which seemed somewhat swollen (fig. 1); in other cells a definite eccentrically placed clear area could be seen which was entirely free from granules and contained only dustlike particles in marked contrast to the rest of the cytoplasm. These changes were not uniform, however, for many of the cells showed no change from the normal. The neurofibrils were broken up to form a granular sediment in the cytoplasm in some of the cells, while in others they could be traced intact through the cell. Eccentricity of the nucleus and some swelling of the cell body completed the typical picture. We were able to detect no change that might be considered as characteristic of the disease, the conditions observed being present in chromatolysis due to any cause. No pigment granules of any character were found in sections of the spinal cord.

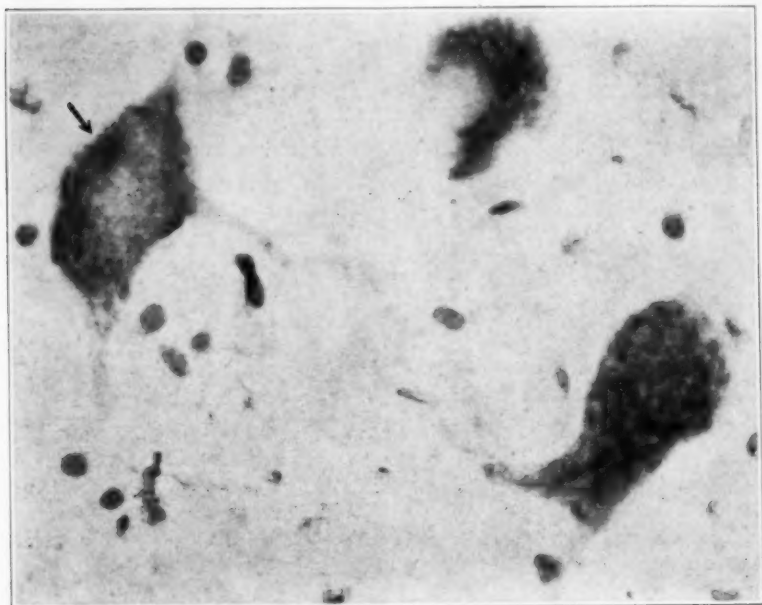


Fig. 1.—Chromatolysis in anterior horn cells, showing variable effect on nerve cells. One is practically unchanged, another shows an eccentrically placed nucleus and the third a loss of tigroid substance in the central portions of the cell. The imperfectly demonstrated nucleolus is seen near the periphery of the cell (arrow). Bielschowsky-Plin method for Nissl's granules; reduced from  $\times 420$ .

In the anterior commissure, just ventral to the central canal of the cervical cord, a small circumscribed area of proliferating glia cells was observed (fig. 2). With phosphotungstic acid hematoxylin, the nuclei were found to be embedded in a tangled mass of glia fibers (fig. 3). This localized proliferation may have been a coincidental observation rather than one due to the disease.

The peripheral nerves showed the most marked changes. In the hematoxylin and eosin and myelin sheath preparations, vacuoles of various sizes were observed which seemed to involve the entire trunk of the nerve fibers, more or less symmetrically (fig. 4A). With the preparations for fat these "vacuoles" were

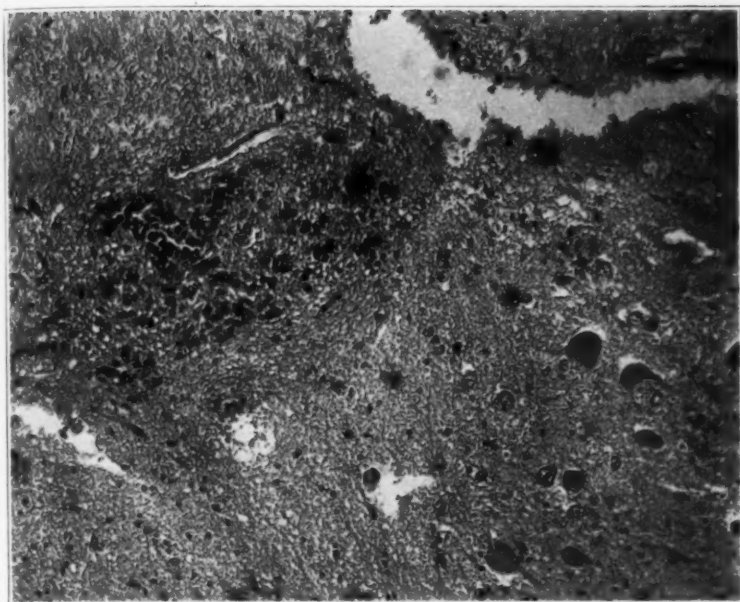


Fig. 2.—Area of gliosis in anterior commissure. Chromatolytic change in the ganglion cells of the anterior horn is also shown, the tigroid substance when present being confined to a narrow ring of cytoplasm in the peripheral portion of the cell. Hematoxylin and eosin stain;  $\times 200$ .

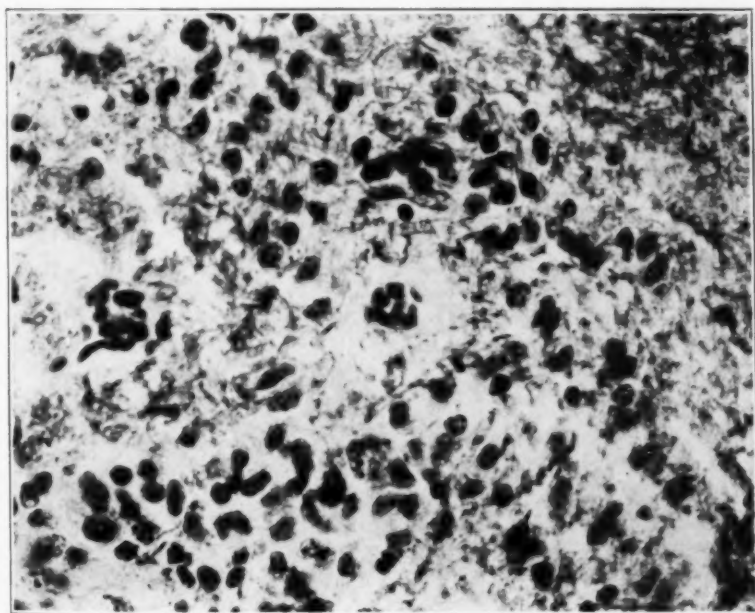


Fig. 3.—Area of gliosis. Glia fibers shown in the mass of cells. Phosphotungstic acid hematoxylin;  $\times 420$ .

found to be globules of fatty material, resulting from the breaking up of the myelin sheaths (fig. 4 *B*). These globules were of a deep purplish color with the Nile blue method and were evidently of the nature of free fat. With the Bielschowsky method, the neurofibrils composing the axis cylinders were found to be intact in most situations, but in some localized areas they seemed to have undergone a process of solution and the usually clearly outlined axis cylinders were replaced by an irregular mass of black granules. There was nothing to indicate the exact cause of the process. The interstitial tissues of the nerves seemed to be free from any proliferation of connective tissue, and wandering cells were not observed. Pigment was not found in any of the sections of the nerves.

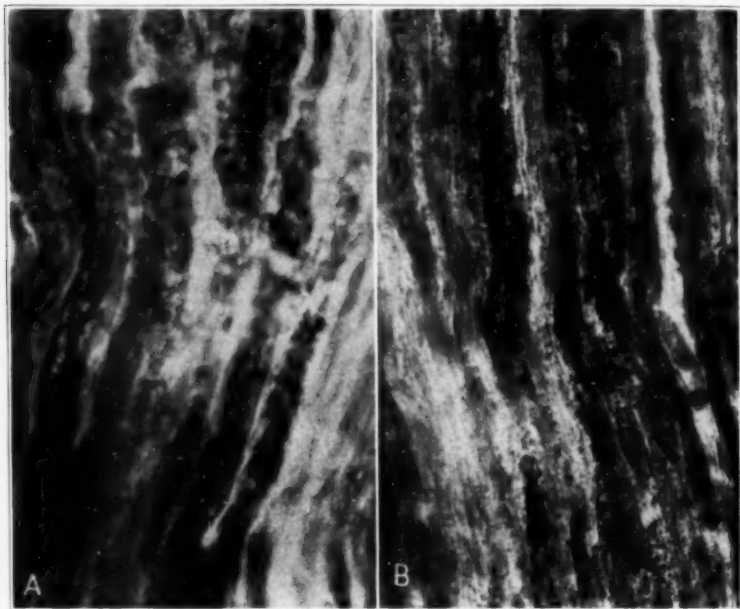


Fig. 4.—Degeneration in the peripheral nerves. *A*, vacuolization of fibers. Modified Wright's stain for myelin sheaths;  $\times 680$ . *B*, globules of fat marking course of the nerve fibers. Nile blue sulphate method for fat;  $\times 320$ .

#### COMMENT

The patient presented the characteristic symptoms of acute, idiopathic hemato-  
porphyria and died in the first attack. There was no family history of the dis-  
ease. Alcoholism and exposure to lead could be excluded, and no drugs had been  
administered until after the onset of symptoms of the disease. Unfortunately,  
careful examinations of sensation could not be made on account of the patient's  
mental condition. There was a marked toxic psychosis, with visual and auditory  
hallucinations and later apathy and coma. Motor weakness of the legs and arms  
and eventually a bulbar palsy developed. The sphincters were disturbed only  
during the last few days before death. The alterations of the nervous system  
consisted of a moderate degree of chromatolysis of the ganglion cells of the  
spinal cord together with marked degeneration of the peripheral nerves.

Porphyrin is a normal excretory product of human beings and is present in the urine, feces and bile. It is also present in meconium. In a number of disease states, it may be excreted in slightly increased amount. Under these circumstances it may be assumed that the disturbed metabolism is responsible in some manner for the increased output of porphyrin. There are a number of reported cases, however, in which the striking feature was the excretion of urine of Burgundy wine color, containing abnormal quantities of hematoporphyrin. Günther,<sup>1</sup> in 1911, and again in 1922, collected all the known examples of the malady and gave it the name "hematoporphyrin." He demonstrated that the anomaly of metabolism is occasionally congenital and rarely hereditary and is, therefore, on a constitutional basis. The cases fall readily into three groups: (1) congenital hematoporphyrin, which appears at birth or in early life and is characterized by dermal photosensitivity and hydroa aestivale; (2) acute toxic hematoporphyrin due to abuse of barbitol (veronal), sulphonal and allied drugs; (3) acute idiopathic hematoporphyrin.

A complete discussion of all phases of the disease may be found in articles and monographs by Günther,<sup>1</sup> Garrod<sup>2</sup> and Borst.<sup>3</sup> We shall discuss here, briefly, only the acute idiopathic type of the disease.

Up to the present time about twenty-four cases have been reported. Males and females have been about equally affected. The disease usually makes its appearance in the second or third decade, but exceptions are frequent. The first symptom is, as a rule, acute, severe, cramplike abdominal pain accompanied by constipation and vomiting. There is often slight fever and a moderate leukocytosis. The urine is dark red or brown and contains hematoporphyrin and urobilin. Roentgen examination often discloses that some part of the intestinal tract is dilated. In the milder attacks these symptoms may ameliorate, with recovery. In more than 50 per cent of the cases evidence of grave damage of the nervous system appears. Delirium and coma have been frequent. Epileptiform attacks, symmetrical radial paralysis, amaurosis, ptosis and optic neuritis have occurred. In about one half of the fatal cases weakness and slight paresthesias of the limbs appeared and were followed by complete paralysis with loss of tendon reflexes and the development of bulbar symptoms leading to death by asphyxia.

A complete review of the etiology, pathogenesis and symptomatology of the disease has been published by one of us (V. R. M.)<sup>4</sup> in a recent article and will not be discussed here.

The nervous system has been examined in a few instances of acute ascending neuritis with hematoporphyrinuria. Bostroem<sup>5</sup> found extensive degenerative changes of the anterior horn cells without evidence of inflammation. There was no cellular infiltration. The blood vessels were not dilated. There was one, probably agonal, small hemorrhage into the cervical region of the spinal cord. The

1. Günther, H.: Die Bedeutung der Hämatoporphyrine in Physiologie und Pathologie, München, J. F. Bergmann, 1922.

2. Garrod, A. E.: Inborn Errors of Metabolism, London, Henry Frowde, 1923, pp. 136-163.

3. Borst, M.: Untersuchungen über kongenitale Porphyrie, Verhandl. d. deutsch. path. Gesellsch. **23**:353, 1928.

4. Mason, V. R., and Farnham, Russell M.: Acute Hematoporphyrin, Arch. Int. Med. **47**:467 (March) 1931.

5. Bostroem, A.: Ueber toxisch bedingte aufsteigende Lähmung mit Hämatoporphyrin, Ztschr. f. d. ges. Neurol. **56**:181, 1920.

ganglion cells of the posterior horns and of Clarke's columns were normal. In Nissl preparations practically every anterior horn cell was altered. Marchi preparations showed no deviation from normal. The spinal root ganglia were altered, and the capsular cells had proliferated. The brain showed slight hyperemia. The large nerves were not examined. Löffler<sup>6</sup> found no definite significant alterations in a typical case; however, the symptoms from the nervous system were apparently of only three days' duration. Campbell<sup>7</sup> found no alterations in the nervous system. Abderhalden<sup>8</sup> studied the nervous system of Grund's patient and found lesions of a purely degenerative type in the peripheral nerves. Snapper<sup>9</sup> reported a normal spinal cord with chronic degenerative changes in the peripheral nerves. Rothman<sup>10</sup> could find no changes in the peripheral nerves, although marked neurologic symptoms were present before death. These reports all represented examples of the disease associated with evidence of grave disturbance of the nervous system similar to Landry's paralysis. Although these reports were often fragmentary or incomplete, it is apparent that acute hematoporphyrinuria, in the majority of fatal cases, is associated with grave lesions of the nervous system. In the cases reported these have been purely degenerative and limited to the peripheral nerves, the posterior root ganglia and the ganglion cells of the spinal cord. No adequate study of the nervous systems of those patients with neurologic disturbances other than peripheral neuritis has been reported.

The prognosis of acute hematoporphyrinuria is always serious. The presence of any definite neurologic symptoms other than a toxic delirium adds to the gravity of the outlook. Melkersson's<sup>11</sup> patient recovered even after the development of an ascending paralysis with bulbar symptoms. Other patients with peripheral neuritis have also recovered. In a number of instances more than one attack has occurred with an ultimate fatal outcome. In general, the mortality rate has been nearly 50 per cent.

No satisfactory treatment for the disease has been described.

6. Löffler, W.: Ueber Porphyrinurie mit akuter aufsteigender Paralyse, *Cor.-Bl. f. schweiz. Aertze* **49**:1871, 1919.

7. Campbell, Keith: A Case of Haematoporphyrinuria, *J. Ment. Sc.* **44**:305, 1898.

8. Abderhalden, A.: Ein Fall von Porphyrinurie, *Ztschr. f. physiol. Chem.* **106**:178, 1919.

9. Snapper, I.: Kolieken gepaard gaande met Porphyrinurie, *Nederl. tijdschr. v. geneesk.* **64**:1233, 1920.

10. Rothman, P. E.: Hematoporphyrinuria, *Am. J. Dis. Child.* **32**:219 (Aug.) 1926.

11. Melkersson, E.: Un cas de porphyrie aiguë spontanée avec symptômes nerveux, et une brève revue de la question des porphyries, *Acta med. Scandinav.* **63**:153, 1926.

## News and Comment

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### INTERNATIONAL NEUROLOGICAL CONGRESS

Further progress has been made in the arrangements for the International Neurological Congress to be held in Berne, Switzerland, Aug. 31 to Sept. 4, 1931, and detailed plans have been elaborated in order to insure its success. The local committee has been able to enlist the active support of the Swiss government in the furtherance of the Congress. President Haeberlin of the Swiss Confederation has promised to open the official sessions on Monday in the formal gathering that will precede the scientific sessions of the Congress. If by any chance the President is detained by more urgent affairs his place will be taken by the Secretary of the Interior. This should provide a propitious opening for the meeting. The Federal Council of Switzerland has voted a considerable sum of money toward the financial support of the Congress.

An official reception has been arranged for Monday evening, August 31, by the authorities of the city of Berne in association with the government of the canton of Berne. This gathering will be held at the Kursaal Schaezli, which is situated on a hill overlooking the entire city.

Complete arrangements have been made for the excursion to be held on Wednesday, September 2, which will include a tour of Interlaken, the lakes and all other points of interest in the vicinity. This should provide a welcome interruption in the scientific program. A concert and reception have been arranged for the afternoon. The arrangements for the entertainment of the guests and members of the International Neurological Congress at the Kursaal in Interlaken have been made by the authorities of Interlaken and by other local organizations.

The official banquet of the Congress will take place on Thursday evening, September 3; all members of the Congress as well as their guests and friends will be entitled to attend.

On Friday evening, September 4, a more or less informal discussion will be held on the relation between neurology and psychiatry and general medicine. This will take place at the Hotel Bellevue Palace and will be followed by a "smoker."

Attention is called to the fact that all the available accommodations in Berne have been reserved by Thomas Cook and Son, the official travel agency for the Congress. It will be practically impossible for any one to obtain suitable accommodations unless application is made through this company.

Admission to the floor of the Congress will be reserved for members only. Visitors will be accommodated in the gallery. Those interested in neurology and psychiatry who are planning to attend the Congress should apply to the Secretary-General for applications for membership and registration cards at the earliest possible moment. Those interested in the tours to be arranged before the Congress should communicate directly with Thomas Cook and Son, 585 Fifth Avenue, New York.

On account of the large number of papers that have been submitted from various countries, it seems certain that a number of separate sessions devoted to special topics will be held on the afternoons of Tuesday, Thursday and Friday. The programs for these sessions are in process of preparation, and it is hoped that the tentative program may be published by May, 1931.

Those wishing any further information in regard to the Congress should address the Secretary-General, Dr. Henry Alsop Riley, 117 East Seventy-Second Street, New York.

BERNARD SACHS, *President.*

HENRY ALSOP RILEY, *Secretary-General.*

#### PANAMERICAN MEDICAL ASSOCIATION

The Third Annual Meeting of the Panamerican Medical Association will be held in Mexico City from July 26 to 31, inclusive, under the auspices of the Department of Public Health of the United States of Mexico.

The Panamerican Medical Association was organized to maintain and promote a more intimate understanding between members of the medical profession in North and Latin America, and to extend courtesies and show hospitality and attention to representative physicians of the other republics of America who visit the United States. The organization is made up of chapters in various cities in North and South America.

For the purpose of stimulating interest in the Association, a Congress is held once a year; it affords an opportunity to physicians from all parts of the Americas to meet, to present papers and to exchange opinions.

In the coming meeting there will be an attempt to divide the work of the Association into sections. Dr. Theodore H. Weisenburg has been appointed president of the Section on Neurology and Psychiatry. Those who wish to contribute to the program should send in their titles and abstracts to Dr. Weisenburg, 1930 Chestnut Street, Philadelphia.

The time selected for the meeting is particularly delightful for a visit to Mexico. The Ward Line is furnishing special rates.

For further information write to Dr. Conrad Berens, Treasurer, 35 East Seventieth Street, New York.

#### INTENSIVE POSTGRADUATE COURSE IN NEUROLOGY AND PSYCHIATRY IN VIENNA

This course will be repeated from June 30 to July 31, 1931, inclusive. It is held under the auspices of the American Medical Association in Vienna and under the personal direction of Professors Pötzl and Marburg.

## Abstracts from Current Literature

ALGOMYOCLONIC ENCEPHALITIS WITH MARKED HYPERALBUMINOSIS OF THE SPINAL FLUID AND OCULAR MYOCLONIA: DISCUSSION AND DIAGNOSIS. JEAN REBOUL-LACHAUX and N. BRAVINSKY, *Rev. d'oto-neuro-opt.* 8:81 (Feb.) 1930.

The clinical picture of the case on which this study is based is that of epidemic encephalitis, but the changes in the spinal fluid—hyperalbuminosis, albuminocytologic dissociation and red blood cells—suggest meningeal hemorrhage associated with the encephalitis and due to the same virus. The relation between epidemic encephalitis and meningeal hemorrhage is not yet well established.

A man, aged 18, was ill in March, 1927, with epidemic encephalitis (fever, headache and vomiting) which lasted for twenty days and was followed by a prolonged convalescence. Recovery was apparently complete, but in September there was another attack, accompanied by hypersomnia, sialorrhea, severe headache and pains in the shoulders, arms and neck. This attack lasted until January and was followed by an interval of two months of amelioration, when another attack supervened. At this time, hypersomnia, horizontal diplopia, psychic excitement, hiccup and painful brachial myoclonia were observed. An examination of the spinal fluid revealed: albumin 3 Gm., 16 lymphocytes and absence of bacteria (especially Koch's bacillus); the Wassermann reaction was negative.

An examination on March 30 revealed: the patient had no fever and was dull and expressionless, the breath was bad, the tongue was dirty and hiccup was present. Both ears were the seat of a chronic suppuration which had existed for ten years. There were a slow, wide clonic nystagmus, irregular pupils, which reacted to light and in accommodation, and no ocular paralyses. In the upper arms there was a rhythmic myoclonus, and in the left arm, the muscular force was diminished and the reflexes were feeble but equal. Diffuse cutaneous hyperesthesia was noted, and passive motion of the arms caused scapular pains. The spinous process of the third cervical vertebra was sensitive to pressure, but roentgenograms did not reveal any vertebral lesion. Myoclonus was present in both legs; the achilles reflexes were present with a tendency to clonus on the left; a typical Babinski's sign was present on both sides; the cutaneous reflexes were unequal, and on the left the cremaster reflex was diminished, and the abdominal reflexes were abolished. The signs of Lasègue and Kernig were marked. The pulse was unstable, from 120 to 160 in rate, the heart sounds were normal and the blood pressure was the maximal 11 cm. and the minimal 6 cm. The urine was normal. Examination of the eyes showed: contraction of the palpebral fissure and myosis in the left eye, nystagmus and normal retina and nerve head, visual functions, motility of the globes and pupillary reflexes.

Injections of sodium salicylate, 1.5 Gm., were given daily, and were followed by some improvement in the clonus, but the patient was completely disoriented. Transient paresis of the legs, cutaneous eruptions, recurrences of the clonias and variations in the state of the mental confusion were present during the following two months. Examination of the spinal fluid on May 5 revealed: slight xanthochromia; albumin, 4 Gm.; chlorides, 7 Gm.; red blood cells; 8 leukocytes; no bacteria; negative Wassermann reaction. Death occurred on June 11.

As to diagnosis, the hypersomnia, myoclonias, algias, diplopia and fever suggested epidemic encephalitis. The marked and increasing hyperalbuminosis with albuminocytologic dissociation in the spinal fluid pointed to intracranial hypertension or compression of the spinal cord from tumor, Pott's disease, etc. The headaches, vomiting and positive Kernig sign suggested meningitis. The bilateral suppurative otitis with grave cerebral signs awakened a suspicion of an otitic intracranial complication. Nystagmus with diffuse pyramidal signs and a bilateral Babinski sign in a young person are elements in multiple sclerosis. The psychic syndrome, confusion, dreamy delirium and amnesia pointed to an infectious or

toxic cortical disturbance. Meningitis, including tuberculous meningitis, could be ruled out from the cytologic picture and the clinical evolution. The diffuse and changing symptoms and the absence of a marked increase in the leukocytes in the spinal fluid and of changes in the eyegrounds are not a picture of otitic meningitis or abscess of the brain. Cerebral tumor and intracranial hypertension were ruled out on account of the absence of papillary stasis, increased spinal fluid pressure (12, Claude) and of slow pulse. The possibility of cervical Pott's disease complicating the encephalitis was seriously considered. But the rapid and complete disappearance of the tenderness of the vertebra, the absence of contractures and the negative roentgenograms removed this suspicion.

The relationship between epidemic encephalitis and acute multiple sclerosis has been suggested by Bériel and Devic and by Anglade, but Guillain and Alajouanine do not agree to this. During the past few years, the attention of neurologists has been drawn to certain toxic-infectious inflammations of the cerebrospinal axis which have an obscure etiology and a bizarre symptomatology. They exhibit a paretic state of the limbs or of the face with a polyneuritic or radicular syndrome and at times pyramidal signs, fever and albuminocytologic dissociation in the spinal fluid, and are curable. The hypothesis of such a condition could not be sustained in the case reported, on account of the absence of true muscular atrophy and objective disturbances of sensibility, the prolonged and fatal course and, especially, the presence of symptoms pathognomonic of epidemic encephalitis.

Certainly it was not a simple type of epidemic encephalitis, but was complicated by algomycoclonic, epidermic, meningeal and psychic phenomena, and especially by the hyperalbuminosis, the albuminocytologic dissociation and the red blood cells in the spinal fluid. The following facts suggest a meningeal hemorrhagic process associated with the encephalitis and due to the same virus: the evolution by successive seizures; the increase of the hyperalbuminosis accompanying a recrudescence of the symptoms and the amelioration following lumbar puncture; the presence of red blood cells in the fluid; clinical signs of meningeal irritation; the analogy of this case with certain facts reported by Cordier, Lévy and Nové-Josserand, by Rathery and Bonnard, by Achard and recently by Léchelle and Alajouanine. The last named writers reported a case with successive meningeal hemorrhages, accompanied by dreamy delirium, amaurosis, sympathetic disturbances, a parkinsonian syndrome and fever, which made the etiologic diagnosis of encephalitis probable. These observations tend to prove that the hemorrhages are often due to hemorrhagic meningo-encephalitis, and that the latter is in certain cases due to the virus of epidemic encephalitis.

DENNIS, Colorado-Springs, Colo.

QUANTITATIVE DETERMINATION OF LIPOIDS IN THE BRAIN. ERIC BACKLIN,  
 Upsala läkaref. förh. 35:105 (June) 1930.

Backlin accepts Overton's definition of lipoids as organic compounds which, like fats, are soluble in one or several of certain organic solvents, especially in benzene and in indifferent narcotics of the aliphatic series, such as ether, petroleum ether, alcohol and chloroform. He also includes among lipoids the sterins, phosphatids and cerebrosides. The sterins and phosphatids are probably found in all living cells and in most body juices. The cerebrosides are also found in many organs and body juices, but chiefly in the brain. In the vertebrate series the only sterin found is cholesterol. Of all phosphatids described thus far, the only ones that can be definitely regarded as such are: lecithin, cephalin and sphingomyelin. Lecithin and cephalin are found together in the organs and juices of the body, and their composition and chemical properties are so similar that it is extremely difficult to isolate them; it is doubtful whether a pure preparation of cephalin can ever be obtained. Sphingomyelin occurs in large quantities in the brain and in smaller amounts in other organs; it is always found together with the cerebrosides with which it has many properties in common. Depending on the fatty acid rest contents there are distinguished four different cerebrosides: (1) phrenosin, (2) kersin, (3) nervosin and (4) an "unnamed cerebroside."

In addition to these principal lipoids there also exists a group of these compounds known as sulphotids (partly phosphorus-containing and partly free from phosphorus).

Whereas the qualitative determination of the various lipoids has within recent years assumed a definite character, their quantitative determination has yielded results that are uncertain and extremely unsatisfactory. All quantitative determinations of the various lipoids in the brain may be said to consist of two processes: (1) an introductory process that concerns itself with the drying of the tissues to be examined and the extraction of the lipoids or groups of lipoids, and (2) the concluding process in which the quantities of the individual isolated lipid or lipoids are determined.

The author subjects to a critical review all methods (macroscopic and microscopic) hitherto in vogue for the quantitative determination of lipoids, and concludes that none of them is of any definite value, except perhaps the method for the determination of the quantity of cholesterol. He then describes his new micromethod of quantitative determination of which the chief advantage seems to be that precise determinations can be obtained from small amounts of tissue. For obvious reasons the chemical procedures of the method as described by the author cannot be abstracted in this review. These must be read in the original paper.

He employed his method to determine quantitatively the amount of water and lipoids in the brains of fifteen guinea-pigs varying in age, but of the same race. The lipoids determined were: cholesterol, nonsaturated phosphatid, saturated phosphatid, cerebrosides with nonsaturated fatty acid radicals, and cerebrosides with saturated fatty acid radicals.

From these experiments he concludes that: 1. During extra-uterine development there is an increase in the dry substance content of the brain. 2. With this increase there is also a proportionate increase of lipoids. 3. There is an increase in all lipid fractions in relation to the fresh brain substance. 4. This increase is relatively smallest for the phosphatids, a fact recognized by their stationary or diminished quantity in their relation to the dry brain substance. 5. The cerebrosides represent quantitatively the most characteristic course of chemical development; they occur only in small traces during birth but later are, relatively speaking, enormously increased, so that they correspond to the diminution in the amount of the phosphatids in the total lipid complex. This behavior of the cerebrosides is due to the fact that they are chiefly developed in connection with myelinization and constitute an important component of the myelin sheaths.

According to Backlin, this process which occurs principally in the white matter plays a significant rôle in the change that takes place in the mixture of gray and white matter during development. His analyses of the gray and white matter from the brain of an adult guinea-pig seem to show definitely that the composition of the gray matter in its relation to the water content and quantity of lipid and individual lipid fractions in their relations to fresh and dried substance, and to the proportion of the total lipoids approaches more closely to the composition of the whole brains of guinea-pigs in their first weeks of development, whereas the corresponding figures for the white matter approach nearer those obtained from adult animals.

KESCHNER, New York.

ASSOCIATED PARALYSIS OF THE GAZE IN A MAN WITH PARKINSON'S DISEASE.  
ANDRÉ-THOMAS, HENRI SCHAEFFER and PROSPER VEIL, *Rev. d'oto-neuro-opht.* 9:178 (March) 1930.

The clinical study of paralysis of associated movements of the eyes and especially vertical paralysis of the gaze has scarcely advanced since 1883, when Parinaud wrote his celebrated memoir. There is still the same uncertainty about the relative symptomatic value of global and dissociated ocular paralyses, and the same ignorance about the existence or nonexistence of supranuclear centers and the exact seat of the cortical centers.

A man, aged 64, had always been well except for a slight trembling of the right hand. In March, 1929, he had painful headaches soon followed by vertigo, ptosis of the right lid and diplopia, which were relieved by injections of cyanide of mercury. When seen in July, he kept the eyes half closed on account of photophobia and the secretion of tears. He exhibited a paralysis of the elevator muscles, and when urged to look upward, there was no contraction of the right brow or lid. When the eyes were energetically closed, the globe did not turn upward, but irritation of the cornea caused the eye to turn upward under the lid. There was paralysis of the "levator." On voluntary movement to the left, neither eye passed the median line; when a point was fixed and the head turned, the right eye alone moved to the inner canthus. In the caloric test of the labyrinths, nystagmus occurred; but while on irrigating the left ear the nystagmus jerks to the right passed the median line, on irrigating the right ear the jerks to the left did not pass it. The pupils were equal and responded slowly to light; visual acuity and the eyegrounds were normal. A parkinsonian syndrome was present. The facies was amimic and there was intention tremor in the right arm and hand. There was no noticeable ataxia or asynergia. The achilles reflexes were abolished, the knee reflexes were diminished and the abdominal and cremaster reflexes were normal. The Wassermann reaction of the blood and spinal fluid was negative.

*Comment.*—1. The ocular troubles followed extrinsic paralysis of the right third nerve, which is notable in Parinaud's syndrome. Léry has stated that in almost all cases of vertical paralysis the third nerve is more or less involved.

2. When voluntary effort to raise the eyes was made, the globes did not pass the horizontal and the lid and brow were not raised. In making the test for Bell's sign, the orbicularis did not contract, and when asked to look to the left the patient did not turn the eyes or head to the left. The question arose as to whether there was not a psychic factor present.

3. The vertical paralysis was dissociated; it affected the voluntary movements but not all the automatic ones, since irritation of the cornea caused the globes to turn up. This fact sustains the opinion that all so-called automatic movements are not the same; between frankly voluntary and undoubted automatic movements there are many gradations.

4. In voluntary movement to the left, neither eye passed the midline, but in the automatic movement the right eye made the full excursion, while the left eye did not go beyond the center.

5. The seat of the lesion is manifestly mesencephalic—probably a disease of the internuclear fibers uniting the oculomotor nuclei with each other and to those of the eighth nerve. The observations in this case speak against the assumption that there are two kinds of vertical paralysis, one global, of mesencephalic origin, and the other dissociated, affecting only the voluntary movements and due to a cortical lesion or to a bilateral attack on the corticonuclear tract.

6. The association of functional paralysis of gaze and the parkinsonian syndrome is unusual. The question as to whether this was a true parkinsonian disease or a syndrome due to vascular lesions of the central nuclei is not determined. The suspicion is aroused, in spite of the negative Wassermann reaction, that syphilis is at the bottom of the trouble. The association of a parkinsonian syndrome, preceding the ocular difficulties, with a double paralysis of function is so exceptional that the bonds uniting them cannot be determined.

DENNIS, Colorado Springs, Colo.

THE COMPARATIVE ANATOMY AND EMBRYOLOGY OF THE HYPOTHALAMIC CENTERS IN LOWER MAMMALIANS AND IN MAN. E. GRÜNTAL, Arch. f. Psychiat. 90:216, 1930.

The structure of the hypothalamus was studied in an ascending series of mammals: bat, mouse, rabbit, calf, cat, dog, monkey and man. The investigation was conditioned by the fact that in studying the hypothalamus of the dog the

author discovered that this structure was much more complicated and more highly differentiated in this animal than in man. This suggested a possibility that a still further increase in differentiation may occur as one descends the scale of mammals. The investigations have shown this actually to be the case; they may be summarized as follows: (1) The hypothalamus increases in differentiation as one descends the scale of the mammalian brain. Although the structure of this body does not seem to show much difference in members of a subclass, it differs remarkably in the different subclasses. For instance, the hypothalamus of the dog and the cat shows a great deal of similarity, but differs fundamentally from the structure of the hypothalamus of rodents, etc. (2) A certain number of components and features of the hypothalamus seems to run through the whole series. The number of nuclei is lowest in the human hypothalamus, in which there is a group of three nuclei in the oral part and a group of four in the caudal end; in the region between the two there are only two nuclei in the inferior part. Of the nuclei, the oral and caudal groups of the human hypothalamus seem to run through the whole series and occupy a more or less constant position, so that these two groups can be looked on as composing the fundamental structure of the hypothalamus. The structures that are placed in the center of the body differ in the different groups. When one compares the hypothalamic structures in the different animals of this series, one finds that there is more in common between the hypothalamus of the cercopithecus (monkey) and that of the dog than there is between that of the monkey and of man. Again, the hypothalamus of the mouse shows a great many similarities to that of the bat.

The author recognizes three types of structure of the hypothalamus in his series. The most highly differentiated and most complex is in the mouse and the bat. The next group is that of the dog and monkey, and the third is that in man which represents the least differentiated and simplest of the series. A study of the hypothalamus in human embryos shows that in the early stages of development the hypothalamus of man is much more complicated than in the adult. It would seem, therefore, that both ontogenetically and phylogenetically the hypothalamus develops in a fashion that is directly opposite to that of the thalamus and the cortex. As a result there is a rather striking difference in proportion: In the mouse there are thirty-two components in the hypothalamus as compared with fifty-five fields in the cortex; in man there are nine components in the hypothalamus and several hundreds of fields in the cortex.

The author points out that these observations should serve as a warning against the readiness with which physiologic and anatomic observations in animals are applied to homologous structures and functions in man. He indicates also the possibility of speculating as to the relative importance of these structures in the different animals. It would seem as if the higher differentiation of the hypothalamic centers, which by some neurophysiologists are considered to be associated with the instinctive life of the animal, would speak for a more autonomic function in lower animals and a less independent one in man.

MALAMUD, Iowa City.

DIAGNOSIS OF INTRACRANIAL TUMORS BY SUPRAVITAL TECHNIQUE. LOUISE EISENHARDT and HARVEY CUSHING, *Am. J. Path.* 6:541 (Sept.) 1930.

The supravital technic has been adopted by the authors as a favored routine method of making pathologic diagnoses of tumors of the nervous system. In this procedure, as devised by Sabin for the examination of the blood, the tissue is neither fixed nor frozen, but simply prepared as a fresh smear of living cells. A small fragment is placed on a glass slide, stained with neutral red dye, and spread by pressure on the cover glass. It is then sealed with a mixture of paraffin and petrolatum, and examined microscopically in a warm box. The preparation of the specimen takes less than a minute.

With experience, immediate diagnoses can be given to the surgeon so that he may learn to associate the microscopic type of the lesion with its gross appear-

ance at the operating table. The method is of particular value in the cytologic differentiation of the various types of gliomas. Descriptions are given of the microscopic appearance of the more common intracranial tumors when examined by this method. The fibrillary astrocytomas are characterized by a network of neuroglia fibrillae which appear as crisscrossing refractive processes among which are scattered nuclei. In less dense areas well preserved astrocytes with long processes extending in starlike fashion from the cell body are distinctly seen.

The protoplasmic astrocytomas do not show a fibrillary network. They tend to undergo degeneration, and numerous vacuolated cells may be present. Astrocytes with intact, soft, branching processes may be seen.

In the glioblastoma multiforme one may readily identify cells of various sizes and shapes, including spongioblasts, astrocytes and multinucleated cells. Mitotic figures are easily recognized. These tumors are frequently necrotic, the tissue being composed largely of huge vacuolated cells filled with greenish, refractive globules, among which are active clasmatocytes. Myelinated nerve fibers are usually present in the invasive lesions, and appear highly refractive.

The medulloblastomas present a distinctive picture. They are composed of masses of cells. In fixed preparations the cytoplasm of these cells may be indiscernible. In supravital preparations the cytoplasmic boundaries are sharply defined and the nuclei unshrunk. The cells are round rather than carrot-shaped. Mitoses in various phases are numerous. Clasmatocytes may be abundant.

In the oligodendrogliomas, also, the appearance of the cells in fresh smears in contrast to fixed preparations is remarkable. In the supravital preparations the spherical nuclei are unshrunk and are surrounded by a ring of pale cytoplasm which is distinctly outlined.

The pituitary adenomas may be differentiated into chromophobe and chromophile types, the alpha granules being readily identified by this method.

The meningiomas as a rule are unmistakable, and whorl formation is well preserved. The oval or round nuclei with prominent nucleoli have a singularly typical appearance. Psammoma bodies appear as round, refractive bodies.

The acoustic neurinomas are recognized by their typical architecture, with fibrillary strands and whorls, and nuclei in palisade arrangement. Occasionally the cytoplasm of the tumor cells is finely vacuolated.

The descriptions are illustrated by a series of photomicrographs comparing supravital preparations with sections of fixed tissue from the same tumors. The supravital method makes it possible for the examiner to see the cells with their cytoplasm and processes intact and gives pictures which are wholly unfamiliar to those who have studied these cells only in fixed sections.

EISENHARDT, Boston.

THE PATHOGENESIS OF OPTIC ATROPHY IN OXYCEPHALY. J. NORDMANN, *Rev. d'oto-neuro-opht.* 8:1 (Jan.) 1930.

A report of this case was published previously and this time is limited to the state of the eyes. The left globe projected more than the right, and both exhibited intense nystagmus. The anterior segments were normal, and the pupils reacted well to light and in accommodation. The papillae were a dirty white and somewhat irregular, and the caliber of the vessels was normal. In the periphery of the right eyeground, there was a spot of pigment. Vision in the right eye was reduced to movements of the hand at 20 cm., and in the left eye it was 5/5. In the left eye there was a concentric reduction of the visual field and a central scotoma for green and red.

The theories of the pathogenesis of optic atrophy in oxycephaly may be reduced to three hypotheses: compression of the nerve, infection and optic neuritis or intracranial hypertension and papillary stasis. The compression theory is based on the observation of narrowed optic foramina, the penetration of the optic canal by the carotid artery, dilatation of the third ventricle, enlargement of the hypophysis and traction on the optic nerve from deepening of the middle fossa. Compression

of the nerve at the base of the cranium almost always produces simple, not gray, atrophy; optic atrophy in oxycephaly is usually postneuritic; simple atrophy is found in only from 10 to 15 per cent of the cases.

The question to resolve is whether hypertension or infection produces the optic atrophy. Papillary stasis may accompany infectious and hypertensive processes, but it is, at least in the beginning, a noninflammatory edema. The conservation of good visual acuity while stasis exists and the noninfectious character of the intracranial hypertension suggest the absence of inflammatory elements in the optic nerve.

In a careful study of the cases reported by 150 writers, the author did not find certain signs of infection in any, although hypertension was frequently noted. This causal hypertension is due to disproportion between the growing brain and the rigid osseous skull. The author concludes that: 1. The optic atrophy of oxycephaly is, in the great majority of cases, a gray atrophy. 2. Compression of the optic nerve usually causes simple atrophy, and, therefore, does not explain the optic atrophy in oxycephaly. 3. The theory of isolated infection is not based on clinical fact but on a single questionable anatomic observation. 4. The optic atrophy probably is the consequence of a papillary stasis arising from intracranial hypertension because: (a) signs of hypertension are found constantly, (b) it has been demonstrated in some cases that this hypertension is aseptic and (c) cases of papillary stasis with conservation of good visual acuity certainly exist. (5) To solve this problem definitely, precise and complete clinical and pathologic observations are of the greatest importance.

DENNIS, Colorado Springs, Colo.

THE PSYCHIATRIC ASPECTS OF ENURESIS. FORREST N. ANDERSON, *Am. J. Dis. Child.* 40:591 (Sept.); 40:818 (Oct.) 1930.

In an effort to discover the common etiologic factors underlying enuresis and to offer a rational plan for relief from this condition, Anderson made a careful study of 150 bed-wetting children and 54 children who were free from this complaint. He first reviews the literature, pointing out that the assigned incidence of enuresis among small children often runs as high as 30 per cent; that the opinion as to sex distribution shows a slight preponderance among males, and that there is a widespread belief among students of this problem in the importance of physical factors. Among the physical bases emphasized by various authors, Anderson lists cystitis, undernourishment, circulatory disturbances, digestive troubles, high salt diet, mental backwardness, genito-urinary abnormalities and hypotonia of the musculature of the bladder. The measures recommended for relief are as varied as the theories of cause; belladonna is praised as an anti-spasmodic, thyroid as a stimulator of mental backwardness, pituitary extract as a tonic for the vesical muscle, camphor as a genital sedative and restriction of the intake of fluid as a rational prophylactic measure. Epidural injections of physiologic solution of sodium chloride have been mentioned, but Anderson is inclined to think that its effect is largely the result of suggestion. Other procedures reported in the extensive literature of the subject include reduction of emotional excitement, awakening the child at stated intervals, discouragement of sleeping on the back, early habit training, circumcision and exercise of the sphincter.

Careful study of his own series led Anderson to conclude that emotional factors constituted the most significant group of elements in the cause of bed-wetting, and that most of the physical factors mentioned in the literature were of influence through suggestion. Improper habit training and severe parental attitudes are probably responsible for the continuation of the enuresis in many instances. Among the emotional traits found in a disproportionately large group of bed-wetters, Anderson emphasizes timidity, feelings of inferiority, shyness and nail-biting. The intelligence of enuretic children tends to be above the average. Of equal importance are Anderson's negative observations; he demonstrates that duration of gestation, character of birth, race, circumcision, left-handedness, thumbsucking, masturbation

and economic status are of negligible importance in the production of enuresis. Since bed-wetting seems to be largely psychic in origin, psychic measures offer most promise in treatment.

DAVIDSON, Newark, N. J.

INTRACRANIAL CALCIFICATIONS IN ROENTGENOGRAMS. H. BOENING, J. f. Psychol. u. Neurol. **40**:190 (May) 1930.

This contribution is based on a study of the roentgenograms made by the author on 3,300 skulls during four years. He invariably employs Hasselwander's stereoskiagraphs for roentgenologic study of the skull, although he does not deny the value of the simple roentgenogram in some cases. In his investigations, thin platelike calcifications of the falx, visible only when the rays are directed sagittally, were fairly common, but his material did not bear out Albrecht's claims that these calcifications are due to trauma, nor did his cases present any clinical characteristics such as convulsions, headaches, etc. Therefore they are regarded as physiologic, and this, he believes, is in harmony with the results obtained from anatomico-pathologic studies. The calcifications found in the pacchionian granulations described by Schüller, and regarded by him as physiologic, were rare in Boening's material. On the other hand pineal shadows were observed in more than 70 per cent of the cases that were exposed to the rays laterally. Albrecht points out that the tela choroidea of the third ventricle is situated on the upper surface of the epiphysis, and that the "brain sand is to be found normally in this location as well as in the epiphysis. . . ." This may perhaps account for the frequency of the "pineal" calcification shadow in the roentgenogram, as well as for the size and shape of the pineal shadow. Following the observations made by Schüller and Nafziger, the author was able on several occasions to diagnose a tumor displacing the brain stem laterally from the displacement of the pineal shadow. Another site of predilection for depositions of lime in the choroid plexus is in the region of the ventricular triangle and in the inferior horn. Schüller described these calcifications as delicate shadows. Albrecht, as well as the author, diagnosed encephalographically a tumor in this location by a shadow in the ventricular triangle in which the plexus calcification assumed an unusual size. The author refers to Ström, who up to 1921 collected from the literature ten cases to which he added five of his own in which calcium deposits could be demonstrated roentgenologically in genuine tumors (fibromas, endotheliomas, sarcomas, gliomas and tumors of the hypophyseal duct). In 1928, Albrecht, in addition to two post-operative cases of tumor in which owing to calcification histologic diagnosis could not be made, reported also a case of calcium deposition in a "carcinomatous looking epithelial tumor which had undergone fatty and cystic degeneration."

The paper is concluded with reports of twenty cases in which roentgenologic studies of intracranial calcifications were of great aid in the diagnosis.

KESCHNER, New York.

A CASE OF POSTRUBEOLIC BILATERAL EXTERNAL NUCLEAR OPHTHALMOPLÉGIA. PAUL PESME, BOISSERIE-LACROIX and R. PHILIP, Rev. d'oto-neuro-opt. **8**: 187 (March) 1930.

Nervous complications following measles are rare and neuro-ocular sequelae still rarer. Only one case has been reported. A child, aged 8 years, had measles on June 26, 1929, during an epidemic in the school. She was considered well in sixteen days and returned to school, but complained of fatigue and a heaviness in the eyelids. In a few days there was complete ptosis. Examination showed a great deal of depression; the temperature was slightly elevated and the pulse rate was over 100 and regular. There was bilateral ptosis, and the eyes were immobile; the pupillary reactions and the eyegrounds were normal. The legs could be raised, but the movement was sudden. The gait was incoordinate, the feet wide apart, and in walking there were incoordinated movements of the trunk and arms. The tendon reflexes were equal but diminished; there was no Babinski's sign. There were

choreo-athetoid movements of the arms. The pharynx showed no abnormality. The spinal fluid was normal, and the Bordet-Wassermann reaction was negative in both the spinal fluid and the blood. A diagnosis of encephalitis was made and intestinal lavage and injections of brands of sulpharsphenamine and methenamine, alternately, were instituted. After three weeks, improvement began and was complete in two months. An examination made three months after the patient had left the hospital showed complete restoration of the eye movements. The choreo-athetoid movements were still present, but otherwise there was complete cure.

In the presence of these facts, the diagnosis of subacute poliomyelitis was made. The ophthalmoplegia came on late in the convalescence from measles, after the period when encephalitic complications usually occur; to be noted also is the fact that the attack of measles was mild. This appears to be an example of direct action on the nervous system of the measles virus. Other virulent infections, as variola, epidemic encephalitis, poliomyelitis and syphilis, have an affinity for the cutaneous covering and the nervous structure, both derived from the ectoderm. Levaditi has studied experimentally some of these infections and grouped those having common characteristics under the name of neurotropic ectodermoses. This observation shows that neuro-ocular complications of rubeola have a spontaneous tendency to complete recovery.

DENNIS, Colorado Springs, Colo.

OBSERVATIONS ON THE ETIOLOGIC RELATIONSHIP OF ACHYLIA GASTRICA TO PERNICIOUS ANEMIA: III. THE NATURE OF THE REACTION BETWEEN NORMAL HUMAN GASTRIC JUICE AND BEEF MUSCLE LEADING TO CLINICAL IMPROVEMENT AND INCREASED BLOOD FORMATION SIMILAR TO THE EFFECT OF LIVER FEEDING. WILLIAM B. CASTLE, WILMOT C. TOWNSEND and CLARK W. HEATH, *Am. J. M. Sc.* **180**:305 (Sept.) 1930.

To comprehend further the nature of pernicious anemia, studies of the intrinsic factor that is present in the normal gastric juice and of the extrinsic element contained in beef muscle were made. Using similar criteria to that in previous experiments, no effect was noted on either reticulocytes or the total number of red blood cells of six patients when given a mixture of beef muscle incubated with pepsin in the presence of hydrochloric acid. Therefore, peptic hydrolysis by means of pepsin from pigs is incapable of duplicating the results seen with human gastric juice. When beef muscle, incubated with normal human gastric juice and rendered proteolytically inactive by heat, was given to the patient, no effect appeared within the control period. When beef muscle was incubated with normal human saliva and given to a patient, no effect occurred. With carefully controlled technic, a "special" duodenal juice, presumably free from gastric contents, was obtained; this was incubated with beef muscle and administered to the patient. This had practically no hematopoietic effect. From the foregoing data it is concluded that the intrinsic factor is undoubtedly secreted by the mucosa of the normal human stomach.

By a special procedure, beef muscle proteins were isolated from beef muscle and incubated with normal human gastric juice. When given to four patients this mixture gave rise to satisfactory remissions. From this it may be said that in all probability protein or some closely related substance is the extrinsic factor in the reaction between the normal human gastric juice and the beef muscle.

All the experiments support the authors' original conception of the nature of addisonian pernicious anemia as due to a virtual deficiency brought about even in the presence of a diet adequate for the normal person by defective gastric digestion of protein as a result of the achylia gastrica. This virtual deficiency is not produced by a defective diet in the usual sense but by a defect in the patient. Just as in the case of diabetes mellitus the faulty organ is known to be the pancreas, so in addisonian pernicious anemia the authors suggest that it is the stomach.

MICHAELS, Detroit.

SOME OBSERVATIONS UPON THE GROWTH, INNERVATION AND FUNCTION OF  
HETEROPLASTIC LIMBS. S. R. DETWILER, J. Exper. Zool. 57:183 (Oct.)  
1930.

The fore limb rudiment of an *Amblystoma punctatum* embryo was excised, and a corresponding rudiment from an *Amblystoma tigrinum* embryo was grafted on the punctatum host four segments caudal to the normal position for the limb. The *tigrinum* limb on the punctatum host reaches a stage of development in about two weeks which is ordinarily attained by the *punctatum* limb in one week. This delay, however, has no effect on the source of origin of the nerves, which grow caudally from higher levels to supply the *tigrinum* limbs, just as they do when an early developing *punctatum* limb is grafted to the same position. In most cases the *tigrinum* limb is supplied by the fifth, sixth and seventh spinal nerves, and this source is essentially the same as when the *punctatum* limb is grafted to the same position.

In 70 per cent of the cases the grafted *tigrinum* limbs showed movements that were coordinated with the opposite intact fore limb of the *punctatum* host. In twelve cases in which a *punctatum* fore limb regenerated in situ, synchronous movements were observed in the homologous muscle groups of the *tigrinum* graft and the *punctatum* regenerant. The same phenomenon occurs when two *punctatum* limbs are functioning in the same positions, and does not depend on any peripheral nerve connection between the graft and the orthotopic limb. The essential condition for homologous function is that both limbs receive some nerve contribution from the original brachial region of the cord. The same is true in the case of a heterotopic limb.

In cases in which the graft receives only a branch of the fifth (brachial) nerve, the limb may exhibit coordinated movements in its various antagonistic muscle groups. This indicates that when the fifth nerve grows caudally to the graft its fibers may distribute themselves to all muscles of the limb.

Regardless of the extreme overloading of the motor neurons by reason of the greatly increased volume of muscle in the large *tigrinum* limb, no evidence of motor hyperplasias in the motor portion of the cord could be detected. Hyperplasias occurred in the spinal-ganglion cells in response to the increased peripheral field, as has been noted previously.

WYMAN, Boston.

A CASE OF HYSTERICAL MASTOIDITIS. MOUNIER-KUHN; Rev. d'oto-neuro-  
ophth. 8:183 (March) 1930.

A girl, aged 15, was seen on August 22. She complained of pain in the ears for the preceding ten days, fever and loss of appetite; she had lost 2 Kg. in two weeks. For the previous two days the pain had been localized in the left mastoid region. The past history elicited the following facts: Since an attack of diphtheria at the age of 10, there had been a succession of troubles. First, pain in the spine was labeled Pott's disease, and she was kept in bed for a year. This was followed by several weeks of fever and insomnia. Finally, in January, 1929, intense and continuous headaches set in. An operation on the adenoids gave relief for a time, but the headaches returned and visual difficulties appeared. Glasses brought renewed relief until the beginning of August, when there was complaint of pain in the ears and fever. One brother was afflicted with pulmonary tuberculosis.

Examination revealed a normal right ear; the left tympanic membrane was barely rosy, and the left mastoid was sensitive at the tip. The spinal column was supple, and there were no signs of meningitis or vasomotor troubles. The patient was poorly developed. Paracentesis of the left drum was not followed by discharge, but relieved the pains temporarily. The pain returned, accompanied by fever and complaint of poor vision in the left eye. The spinal fluid was normal. An operation on the mastoid revealed no pathologic involvement, but relieved all complaints for three weeks. Then there were complaints of pain in the right ear, fever and insomnia. A neurologist was consulted and advised return to the family life and occupation. Again there was amelioration for a while, and again

the pain in the right ear and fever returned. An injection of procaine hydrochloride over the mastoid gave relief for a week, and then distilled water was equally efficacious. Finally, a pediatrician was called in who was firm enough to impress the patient, and all complaints ceased.

The basis of this complex pathologic process was evidently the emotional shock from the diphtheria. Contrary to previous ideas, the psychic shock of the operation was not sufficient to effect a cure, and recourse to energetic psychotherapy was necessary.

DENNIS, Colorado Springs, Colo.

THE TROPHIC FUNCTIONS OF THE DORSAL INTEROSSEOUS NERVE AND ITS RELATIONSHIP TO EDEMA OF THE HAND. L. A. SHILNIKOV, *Mod. Neuro-psychiatry* (Kieff) 11:7, 1930.

The etiology of chronic edema of the hand was not understood until Molochov's experiments, which demonstrated that this condition was caused by neuritis of the dorsal interosseous nerve. The author is specially interested in the chronic edema of the hand with hyperplasia and sclerosis of the connective tissues, which is commonly known as trophedema of Meige. In typical cases the following symptoms are found: subjective sensations manifest themselves, such as a feeling of heaviness and itching; the edema sets in rapidly; there is a sharp area of demarcation between the affected area and the healthy tissues; in the early stages, the subcutaneous tissues feel soft and jelly-like; in the later stages, the tissues become indurated; there is pitting on pressure; there is a bluish-red discoloration of the skin; the temperature of the affected area is a degree lower than that of the surrounding tissues; the edematous area perspires more profusely and absorbs fluids more readily.

Four cases are reported with the symptoms described. In three, the symptoms appeared after an accident in which the hand was injured. In the fourth case, the patient was a girl, aged 21, whose work consisted in loading peat. Neurotomy of the dorsal interosseous nerve was done, and resulted in the disappearance of the edema within a few days. Within two weeks, all patients were able to leave the hospital, free from symptoms. Following the operation there was also noted a marked change in the metabolism of the affected areas. The test of Aldrich and MacClure gave the same results as in other healthy tissues, whereas previous to the operation there was an increased power of absorption of fluids. The author believes that the operative results are a supporting proof of the theory that the various forms of edema of the hand with subsequent involvement of articular surfaces are due to neuritis of the posterior interosseous nerve.

KASANIN, Boston.

MENTAL HYGIENE AND CRIMINOLOGY. FRANZ ALEXANDER, *Ment. Hyg.* 14:853 (Oct.) 1930.

After expressing admiration, presumably ironical, at the "marvelous organization" of the judicial system in the United States, by means of which criminals are discovered, the psychic roots of their delinquency diagnosed, and satisfactory treatment instituted, Alexander states the belief that psychoanalysis will be valid for the neurotic, for the genius, for the child and for the criminal. Criminal delinquency, he explains, is really a neurosis; it represents a conflict between the instinctive drives of the subconscious and the rational inhibitions imposed by society. When the child fails to make a satisfactory sexual adjustment, this difficulty is carried into adult life; here it is rationalized as an economic problem and thus translated into crime. He cites the astonishing case of a postman whose oral eroticism drove him to excessive cigaret smoking, which in turn led him to opening registered letters to get the money with which to buy cigarets. To the ordinary person this would appear a simple case of stealing to satisfy an economic demand. Alexander, however, condemns this conclusion as being rational,

and therefore, presumably, invalid. The stealing of the money in this case was shown by proper psychoanalysis to be compensation for an oral repression.

Alexander makes the generalization that all instinctive stealing represents a form of oral eroticism. Punishment, he believes, is contra-indicated in neurotic law breaking because the desire for punishment will lure the criminal to repeat his offense; psychoanalysis should be substituted, which apparently will be punishment enough.

Alexander concludes by viewing with alarm the progress of mechanization, which, he says, takes away erotic satisfaction in individual achievement. The world, it seems, is becoming de-eroticized. Society's compensation for this process is the development of moving pictures, sports and chewing gum.

DAVIDSON, Newark, N. J.

THE PROJECTION AND PERCEPTION OF COLOR AND RELIEF. A. QUIDOR and M. HÉRUBEL, *Ann. d'ocul.* **167**:191 (March) 1930.

The psychophysiologic theory which Quidor and Herubel have published (*Ann. d'ocul.* **167**:185 [March] 1930) is verified by an amplification of their study of perception and projection of color and relief. Their method of registering color is similar to the process of Lumière. They conclude from their researches and from the practical application of their work that the theory of Helmholtz, which attributes to the phenomenon of convergence the geometric reconstruction in space of the objects represented by their joined images and which does not admit of monocular perception of relief, is thoroughly contradicted by their experiment and by the facts. As Helmholtz knew, the two retinas contain points that are identical in certain cases and not identical in others. The parallax itself has not the importance which he assigned to it. The results of their experiments enable them to oppose to the objective theory of Helmholtz a subjective theory, or psychophysiologic theory, which recognizes in each one the power or ability to interpret retinal perception in comparing them with cerebral images previously perceived.

The child judges the distance of an object by the effort required to seize it. The authors refer to the fact that people who have been blind from birth and to whom vision is restored find it necessary to develop cerebral images by similar means before they can see well. The number and exactness of cerebral images and the ability developed by their acquisition limit one's intelligence but still permit one the method of adding to their strength by one's own efforts. One's intellectual course depends on past activity. It is a function of personal efforts and is capable of being developed. The development of intelligence, like the development of the body, is governed by activity. In this there is a general law which dominates the evolution of the individual as it dominates the evolution of the species.

BERENS, New York.

TUMORS OF THE OPTIC NERVE. ROY R. GRINKER, *Arch. Ophth.* **4**:497 (Oct.) 1930.

Tribute is first paid to Bailey and Cushing for bringing order into the chaos of the various intracranial neoplasms. A similar chaos exists in regard to tumors of the optic nerve. Regardless of their tissue origin or histogenesis, such terms as fibroma, fibrosarcoma, myxoma, neuroma, glioma and all possible combinations of them have been used repeatedly by various authorities.

A typical case of tumor of the optic nerve is first given as a basis for the paper. Comment is then made on it as an introduction to the pathologic classification which follows.

These tumors are relatively infrequent, the incidence being about 0.84 per cent of all intracranial neoplasms and about 2 per cent of all these gliomas. About 20 per cent of them were both intracranial and intra-orbital. The purely intracranial tumors of the optic nerve are rare. The literature of the histogenesis

is well covered, and does not add confusion as it might well do. The author seems to adhere to Verhoeff's description and gives it as being by far the most complete.

With the exception of two unusual cases reported, all of the tumors seem to be spongioblastomas, with either unipolar or bipolar cells, having one of the following general characteristics: vascular occlusions, cystic degeneration and hemorrhages, the cell being a fusiform one with delicate processes, revealing frequent mitotic figures, some with a coarse and others with a fine reticulum, some showing hyaline degeneration and all with peculiar staining qualities. No differentiation of the spongioblasts into more adult glia in the tumors has been found. Also, following established facts, as quoted at the close of the article, the earlier the cell type in the histogenetic series, the more malignant is the nature of the tumor.

SPAETH, Philadelphia.

AN EXPERIMENTAL STUDY OF THE PATHOGENESIS OF PAPILLEDEMA OF ORBITAL ORIGIN. B. DIMISSIANOS, *Ann. d'ocul.* **167**:33 (Jan.) 1930.

Dimissianos points out that papilledema is not a disease but a symptom caused by varied pathologic conditions. Papilledema is most frequently caused by conditions that increase intracranial pressure and more rarely by lesions that progress without modification of this pressure. In the latter cases the causes are: (1) localized within the cranial cavity (thrombosis of the cavernous sinus [Kampierstein]); (2) in the orbit (tumor and hemorrhage into the sheaths of the optic nerve [Dupuy-Dutemps]); (3) thrombosis of the central vein (Yamaguchi, Marcel Kalt). Papilledema as a result of one of these conditions is evidently of peripheral origin. After briefly reviewing the theories advanced to explain papilledema, fifteen experiments on rabbits and dogs are reported. Paraffin liquefying at from 40 to 45 C. was injected at the apex of the orbit or near the posterior pole of the eyeball. This substance was chosen because it is nonirritating and non-absorbable. In these experiments, compression of the optic nerve in the region of the central vessels was attempted by one injection; the other injection effected compression posterior to the entrance of these vessels into the optic nerve. The idea of injecting in this manner was inspired by a remark of de Wecker, who stated that lesions affecting the posterior part of the nerve only produced atrophy, not papilledema. Dimissianos concludes from these experiments that compression of the central vein close to the eyeball is necessary for the production of papilledema. In a recent discussion in regard to papilledema, which is occasionally seen in multiple sclerosis, Rosenfeld attributed papilledema to the presence of a lesion in the optic nerve close to the eyeball. The author thinks that his experiments sustain the theory of Deyl-Dupuy-Dutemps, namely, that either direct or indirect compression of the central vein or its anastomoses, close to or far from the eyeball, results in papilledema.

BERENS, New York.

MALARIA TREATMENT OF PARESIS. WALTER FREEMAN, *Am. J. Syph.* **14**:326 (July) 1930.

To determine the mechanism of the malarial management of dementia paralytica, Freeman studied the morbid anatomy of the viscera on the theory that if malaria exercised any definite spirocheticidal function, amelioration of the syphilitic pathology should be evident in the nonnervous tissues as well as in the brain. This, however, was not his observation. On the contrary, the manifestations of syphilis elsewhere than in the nervous system were more pronounced in cases that responded clinically to malaria than in those in which fever therapy did no good. This led Freeman to question the alleged spirochete-destroying power of heat. A further challenge to the simple theory of destruction of the spirochetes by heat is offered by the fact that malaria has no influence on primary or secondary syphilis, and by the observation that there is no relationship between clinical improvement and the height of the fever paroxysm. Freeman expresses the belief

that the explanation of malaria therapy does not lie in the heat theory. He advances the hypothesis that the spirochetes protect themselves from the parasitocidal action of wandering cells by making nests in the fibroblastic tissue, and the pooriness of the brain in this tissue robs the spirochete of this defense. In this way the organism can be expelled from the brain by the forced drainage provoked by the fever and by the activation of the reticulo-endothelial system, whereas the spirochetes that are better protected in other viscera by fibroblastic nests do not yield to these influences.

DAVIDSON, Newark, N. J.

OBSESSIVE THOUGHTS IN OCULAR SPASMS. E. STÖRRING, Arch. f. Psychiat. **89**:836, 1930.

The author discusses a group of cases of epidemic encephalitis in which he observed compulsive psychic phenomena in conjunction with ocular spasms. In his analysis of the psychic states accompanying ocular spasms, he considers the phenomena of anxiety and tension as the most elementary components. These two are in his mind closely associated with the occurrence of compulsions. Although this would correspond in general to Stern's conception, the author disagrees with him on the primary quality of the so-called "sticking of thought" phenomena. The author believes that this is really a secondary occurrence. The subjective experience of compulsion develops out of a conflict between the voluntary orientation of the ego and the objective force of the obsessive process. As a result, the patient experiences a feeling of futility and surrender. This process, however, in itself is not primary in that it is preceded by a recognition of the fact that an obsessive act is taking place and also that the patient has developed an increased tendency to self-observation.

This self-observation the author terms the function of "transcendence of consciousness." He considers that this function is present to a certain extent even in normal persons, but is exaggerated to a pathologic degree in these patients. It is because of this that the author does not agree with Stern in the latter's statement that such self-observation denotes a primary splitting of the personality. The increase of the function of self-observation has been attributed by Burger and Mayer-Gross to a state of "peculiar wakefulness." The author considers this concept too as being reducible to an exaggeration of the function of transcendence.

MALAMUD, Iowa City.

ZONA OPHTHALMICA: PERSISTENT MENINGITIS OF LONG DURATION. A. COLRAT, Rev. d'oto-neuro-opht. **8**:449 (June) 1930.

Disease of the meninges in zona ophthalmica follows inflammation of the gasserian ganglion; little is known of the duration. In the case reported, lumbar puncture showed a meningeal reaction fifteen months after the acute stage of zona. The case concerns a man, aged 72, who was attacked with zona ophthalmica, with severe pains, in June, 1928. Interstitial keratitis and loss of vision were noted. Treatment by various means was without avail; lumbar puncture was refused by the patient until Sept. 6, 1929, the pain and insomnia having persisted until then. Tension of the cerebrospinal fluid was normal (25 Claude) and there were five lymphocytes per cubic millimeter. The Wassermann reaction of both the spinal fluid and the blood was negative. Immediate relief was not obtained, but after three weeks the pain and sleeplessness were ameliorated, and by March 6, 1930, the cure was complete. The sequelae were the keratitic infiltration (vision reduced to the perception of light) and almost complete anesthesia in the domain of the ophthalmic nerve.

The duration and intensity of the pains in zona are variable, and the cases with the most intense initial pains do not, as a rule, last the longest. The initial pains are due to meningogasseritis. The causes of the late postzosterian algias are diverse. At times, injections of alcohol into the sphenopalatine or the ophthalmic ganglia, or even around the temporal artery, give relief, which suggests a sympa-

thetic participation. No one method always succeeds. Probably the pathologic process is not the same in all cases. Again, in patients treated simply by analgesics the most lasting algias cease progressively. It can be seen, at least in certain cases, that the late postzosterian pains are due to the persistence of meningogasseritis.

DENNIS, Colorado Springs, Colo.

REMOTE SEQUELAE OF CEREBRAL CONCUSSION. PIGNÈDE and P. ABÉLY, *Encéphale* **25**:436 (June) 1930.

The study concerns a group of patients who may be looked on as "compensation" cases. They came under observation several years after the World War, alleging an aggravation of symptoms but presenting an external appearance of soundness and health. Socially, they are within normal limits. A thorough neuropsychiatric examination, however, gives some real vindication for the claims. A comparatively large series shows a striking similarity in symptomatology.

The history is one of injury without discoverable damage to the cranium. Usually the cause was the force of explosion of projectiles, or falls. There would be confusion for a few hours, up to two days, with superficial wounds of the scalp. Subsequently, there developed the train of symptoms calling for pension or relief. The outstanding elements of this later picture are vertigo and headache. Four detailed case histories are included, with a final summing up of the syndrome in outline form: (1) In the intellectual sphere, amnesia, disturbances of attention, puerilism, extreme fatigability of intellectual processes with perfect conservation of earlier acquired ideas. (2) In the affective sphere, morbid irritability, impulsiveness, emotional instability and disequilibrium, with a tendency to cyclothymic states or occasionally to dipsomania. (3) In the domain of activity, aboulia and diminished occupational capacity. (4) Associated with the symptoms cited are intermittent or continuous headache, vertigo, without any epileptic characteristics, and sympathicotonia,

All of the symptoms are usually found grouped in their totality, though occasionally emotional disequilibrium is lacking. From anatomicopathologic studies it is believed that prefrontal lesions (probably posthemorrhagic) explain the picture in large part.

ANDERSON, Los Angeles.

PSYCHIATRIC EDUCATION. EDWARD A. STRECKER, *Ment. Hyg.* **14**:797 (Oct.) 1930.

Most of the clientele of the general practitioner, at least during his earlier years, consists of frankly neurotic persons or of patients with organic diseases, either active or convalescent, complicated by functional manifestations. The average practitioner has had a psychiatric training inadequate to meet this demand, and as a result, he either fails to recognize the neurotic nature of the illness, or, recognizing it, treats it almost with contempt. Many young physicians have an extensive pediatric practice and have such problems as enuresis, masturbation, running away from home, lying and temper tantrums to deal with. Here, too, his training in psychology has been too meager to give him an understanding of the mechanics of these problems. What little time the schedule of the medical school does allot to psychiatric training is devoted largely to the frank psychoses, a problem that will take up but a small part of the time of the average practitioner. What is needed, Strecker believes, is a revision of the schedule that will give more time to dynamic psychology. He next considers the question of the education of the psychiatric consultant. Intensive training in pathology, endocrinology, psychoanalysis, etc., is neither necessary nor expedient. A thorough grounding in anatomy and physiology is, of course, necessary, yet it should not be carried to the point of crystallizing thought. Graduate work should devote itself to psychiatry and should not overemphasize neurology. Training in psychology should be thorough. Residence in a hospital for patients with mental disorders

or intimate attachment to a psychiatric clinic is, Strecker believes, necessary. Provision should be made for child guidance study. Finally, psychiatrists themselves should set high standards of general cultural training.

DAVIDSON, Newark, N. J.

OCULOGYRIC CRISIS IN POSTENCEPHALITIC STATES. A. E. BENNETT and J. M. PATTON, Arch. Ophth. 4:361 (Sept.) 1930.

As the authors state, "Of all the bizarre residual encephalitic manifestations, probably none is more inexplicable than the oculogyric crisis." The name applies to that syndrome in which spasmodic deviations of the eyeballs occur, either upward, downward or laterally. The eyes may become fixed in one place, frequently with a fluttering or an involuntary forced closure of the lids. These are often accompanied by synergistic movements of the head and body with the attacks. Trance-like attacks may occur, emotional disturbances are not uncommon, and the syndrome is usually seen in parkinsonian states. The emotional attacks have a marked fear and anxiety component. Jelliffe attempted to work out an organic and psychogenic origin for the seizures. As no necropsy studies have been made, pathologic explanations are purely hypothetical, but it seems possible that the pathologic process lies in the basal ganglia or in the striopallidal system.

The authors have reported seven cases in this series. In only one was a history of encephalitis absent, although a typical parkinsonian state was present. In another the encephalitic history was present, but the state of paralysis agitans was absent. The four other patients had histories of encephalitis with a parkinsonian state as a sequel.

The symptomatology in these seven cases is given in good detail. They are also discussed from the standpoint of progress and therapy. Scopolamine and stramonium were the drugs used. Both drugs seemed to give worth while assistance; they seemed, in fact, to permit a formerly incapacitated patient to return to work. No tendency to spontaneous cure was observed in any of the cases.

SPAETH, Philadelphia.

THE MECHANICS OF MIGRATION OF THE DISTAL PIGMENT CELLS IN THE EYES OF PALAEMONETES. JOHN H. WELSH, J. Exper. Zool. 56:459 (July) 1930.

An omatidium of the shrimp, *Palaemonetes vulgaris* Stimpson, is supplied with two pigment cells, each having a distal and a proximal process. These cells form a collar around the cone and move "in" and "out" under the influence of light and dark, aiding in regulating the amount of light reaching the rhabdomes. The folding of the distal pigment cells in the position characteristic for the light is a regular occurrence owing to the contractile elements within the cells. Depigmentation shows the presence of "contractile fibrils" extending from the nuclei of the reticular through the bodies of the distal pigment cells. There is one fibril for each functional reticular cell. The shortening of the fibrils accounts for the proximal migration of the distal pigment cells in the light, while the relaxation of the fibrils, and possibly the contraction of the distal processes, accounts for distal migration in the dark.

Direct measurements of the migration of the distal pigment cells may be made in the dark by brief exposure to weak, red light. Considerable variation in the time required for complete migration is found in different individuals. The average time required for migration in the light is about forty minutes, while about ninety minutes is required in the dark. The rate of movement varies throughout the migration; when the distance migrated is plotted against time in the light or the dark, a sigmoid curve is obtained. Pigment cells that have begun to migrate in the light will continue moving for an appreciable length of time after the animal is placed in the dark.

WYMAN, Boston.

PRECIPITATING MENTAL CONFLICTS IN SCHIZOPHRENIA. G. E. GARDNER, J. Nerv. & Ment. Dis. **71**:645 (May) 1930.

Hoch and Meyer, Bleuler and Sullivan, Boltz and Rosanoff have all emphasized the importance of mental causes of schizophrenia as contrasted with physical factors. Reactions to exacting situations in the early stages may enable one to detect the oncoming disease. Sullivan has described states of so-called depression or unhappiness based on maladjustment to assumed personal inadequacy which have occurred a long time before the outbreak of a frank psychosis. He has drawn attention to two types of precipitating causes, namely, sexual situations and occurrences which arouse strong unconscious wishes. The precipitating cause, as he has expressed it, is the agent which brings to the surface previously submerged cravings. Rosanoff attributed to psychic causes 56 per cent of his schizophrenic cases. Similar conclusions have been reached by Strecker in an investigation of 100 cases of schizophrenia and 100 cases of manic-depressive psychosis. The author studied cases of schizophrenia, 50 in men and 50 in women, at McLean Hospital, Waverly, Mass., and found that nearly 50 per cent of the patients were enmeshed in conscious sexual maladjustments and 25 per cent were facing economic insufficiency and failure. Deep feelings of guilt, inadequacy and incompetency are the most general mental states concomitant with the onset of a schizophrenic disorder developing in personalities unable to accept frustration, defeat or censure of other human beings.

HART, Greenwich, Conn.

THE TREATMENT OF STRABISMUS BY INJECTION OF ALCOHOL. G. SALVATI, Ann. d'ocul. **167**:229 (March) 1930.

The correction of strabismic deviation, especially if it is performed solely for the esthetic result, is usually obtained by suppressing the action of the overactive muscle by tenotomy. Salvati points out that tenotomy may cause functional disturbance, particularly in young subjects, by secondary deviation in the opposite direction. Sinking of the caruncle and enlarging the palpebral aperture by a slight degree of exophthalmos is disfiguring. He has weakened the action of the overactive muscle by injections of alcohol along the course of the muscle, with the hope of paralyzing the motor endings. For this purpose he uses absolute alcohol with the addition of several drops of procaine hydrochloride. This may be a practical procedure, especially when patients object to surgical measures or when an operation has resulted in undercorrection.

Technic: After local anesthesia, the tendon of the muscle is seized close to its scleral insertion and a needle, 2 cm. long, is inserted parallel to the plane of the muscle. Injection, which is painless, is begun immediately and continued as the needle is pushed backward until 2 cc. have been injected. This is followed on the next day by chemosis of the conjunctiva and eyelid which rapidly disappears. After two or three days, the eye is in its normal position. If a single injection is not sufficient to obtain a good result, a second injection may be administered a week later.

BERENS, New York.

THORACIC SYMPATHETIC CARDIAC NERVES IN MAN. A. KUNTZ and A. MOREHOUSE, Arch. Surg. **20**:607 (April) 1930.

Although it is conventionally considered that the sympathetic nerve supply of the heart is limited to fibers from the cervical sympathetic cord, Kuntz and Morehouse believe that they have established the existence of nerves from the thoracic area. Their experiments consisted of careful dissections of human subjects. The nerves they found ran from the medial side of the upper thoracic ganglia of the sympathetic trunk and reached the heart either by way of the deep cardiac plexus or by anastomosis with the cervical sympathetic cardiac nerves coming from above. These nerves were largely postganglionic, although some medullated fibers suggested that visceral afferent impulses might travel this way also. The efferent function of these thoracic sympathetics is, the authors believe, in part or in whole cardiac acceleration. The clinical value of the work

is the relief afforded to surgeons who hesitate to remove the cervical sympathetic ganglia for vascular diseases of the upper extremity because they are afraid of depriving the heart of its sympathetic mediation. Kuntz and Morehouse believe that such a procedure would still leave the heart with some sympathetic supply by way of these thoracic fibers.

DAVIDSON, Newark, N. J.

CONTRIBUTION TO THE KNOWLEDGE OF BRAIN CYSTS AND THEIR DEMONSTRATION BY MEANS OF ENCEPHALOGRAPHY. O. WINTERSTEIN, Schweiz. Arch. f. Neurol. u. Psychiat. **26**:41, 1930.

Winterstein reports a case of posttraumatic epilepsy in which a left hemiplegia developed and in which the patient remained unconscious for four weeks following a skull fracture. Improvement followed and the patient was finally able to return to work, but eight months after the injury, generalized convulsions, preceded by clonic spasms of the left arm, appeared. The patient also complained of paresthesias of that member. Encephalograms, excellent reproductions of which appear in the article, revealed a hydrocephalus internus, distortion of the right lateral ventricle and a collection of air in the base of the right middle fossa, which was interpreted as a cyst in the temporal lobe communicating with the inferior horn of the ventricle. At operation a subarachnoid cyst lying over the right motor area and a cyst of the temporal lobe were drained. A complete hemiplegia developed following the operation, and the patient died of pneumonia ten days later. At autopsy an extensive hemorrhage was found in the right cerebrum, caused apparently by the exploring trochar.

In spite of its danger, the author believes that encephalography is indicated in selected posttraumatic cases, since ordinary clinical methods usually do not suffice to demonstrate the presence of cysts that may be amenable to surgical treatment.

DANIELS, Rochester, Minn.

SYNDROME OF THE CAUDA EQUINA (FOLLOWING ON THE DOUBLE MECHANISM OF ELONGATION AND TORSION). J. TRABAUD, H. SABAH and A. TABAH, *Encéphale* **25**:444 (June) 1930.

The case reported is considered worthy of record because of the rarity of the mechanism involved. The patient had been struck on the head and neck by a large pile of lumber. He was found doubled over, his face folded against his feet. Following twelve days of coma, he progressed soon to essentially the condition in which he has remained for a long time. There was no roentgen evidence of fracture or subluxation. The symptoms were the following: bilateral atrophy of the lower limbs, which was more marked on the right; preservation of voluntary activity of the legs, although diminished in power; absent achilles with preserved knee jerks; disturbed sensation corresponding to a radicular distribution of the third to the fifth sacral, inclusive, in toto and of the first and second sacral in part; disturbances of bladder, bowel and genital function. The case is curious in view of the severe trauma without symptoms of injury to the spinal cord itself—all of the injury was to the nerves. The only explanation appears to be in the minimum amount of "play" permitted between the meningeal and bony attachments.

ANDERSON, Los Angeles.

CLINICAL FEATURES AND PATHOLOGIC ANATOMY OF THE ACUTE ASCENDING PARALYSIS OF LANDRY. E. M. PAWLJUTSCHENKO, Arch. f. Psychiat. **89**:570, 1930.

The author reports the case of a woman, aged 24, whose family and previous histories were unimportant except for an indication of underdevelopment of the vascular and lymphatic systems. Following an acute follicular angina, a rapidly progressing ascending paralysis developed without symptoms in the pyramidal tract or muscular atrophy, but with disturbances of sensation and of the pelvic viscera. The autopsy revealed a diffuse involvement of an inflammatory type affecting the brain, cord, roots, peripheral nerves and meninges. This was especially

pronounced in the roots of the nerves and the spinal cord, especially in the region of the lumbar and sacral segments. There was also a marked involvement of the subthalamic region. Bacteriologic examination revealed the presence of diplococci and streptococci. A culture from the cerebrospinal fluid gave negative results.

On the basis of this case and others reported in the literature, the author reaches the following conclusions: 1. This disease has a characteristic clinical picture, but may be due to different factors. Because of this the anatomic changes are not always the same. 2. The symptomatology of the disease is closely related to its mode of spreading, which should be regarded as lymphogenic, with a primary location in the roots.

MALAMUD, Iowa City.

PARALYSIS OF AN EXTRA-OCULAR MUSCLE AFTER SPINAL ANESTHESIA. JOSEPH LEVINE, *Arch. Ophthalm.* 4:516 (Oct.) 1930.

The occurrence of paralysis of an extra-ocular muscle following spinal puncture or connected with spinal anesthesia is fortunately rare. Still, it is too common a complication not to be considered seriously. As the author quotes, Blatt reviewed a series of eighty-eight cases, Mühsam a series of six cases, Dameno a series of four cases and Reber a series of seven cases, Landon, Minazzini, Scheppens, Gontermann, Balbuena, Merle and Frogé and Moore also reported single instances of either bilateral or unilateral involvement. In most of them, the external rectus was involved. The various theories as to the causative factor in these paralyses are discussed. The frequency of an involvement of the sixth nerve and the fact that its nucleus is most basal in position seems to give a clue to the etiology. It is probably one of toxic nature arising from the catabolism of the various drugs used, i. e., benzoldimethylaminoethylpropenol hydrochloride, procaine hydrochloride, tropococaine and perhaps cocaine. The analogy between this condition and that of postdiphtheritic paralysis is plausible. The nature of the application of this toxin is also not difficult of conjecture. A meningeal irritation is probable, since the involvement of the roots of the vagus and glossopharyngeal nerves (which is not uncommon) points to an easy involvement of other superficially placed centers as well.

SPAETH, Philadelphia.

ENURESIS. CARL POTOTZKY, *Am. J. Dis. Child.* 40:46 (July) 1930.

General exercise for developing will power should be used in the management of enuresis of the type that Pototzky designates as "psychopathic." Unfortunately the author does not describe any exercise for developing will power. Other characteristics of this form of bed-wetting are indifference, fright, spite, abnormally deep sleep and some subconscious force such as an Oedipus or an inferiority complex. This child should be awakened during each night and encouraged to void. Suggestion of the kind advised by Coué is also recommended by Pototzky, who suggests that the child say aloud: "I will keep dry." Not all cases of enuresis are classified as psychopathic; other types include the neuropathic, endocrine and fetalistic. The neuropathic type is represented by the hypersensitive child in whom simple stimuli such as cold, fear, shaking, laughter, etc., are adequate to cause bed-wetting. For these children, quiet and peaceful sleep is essential even if a sedative has to be used to obtain it. Pototzky strongly recommends camphor for this purpose. Children who have enuresis of the fetalistic type show disharmony of development; they should be treated with calcium, vitamins and tonics. Finally, cases of enuresis with a definite endocrine disturbance exist and should be corrected by proper glandular therapy.

DAVIDSON, Newark, N. J.

PAPILLEDEMA. CRITICISM OF THEORIES. L. DUPUY-DUTEMPS, *Ann. d'ocul.* 167:134 (Feb.) 1930.

Dupuy-Dutemps criticizes the theories of papilledema based on the extension of edema from the brain or as the result of blocking lymphatic drainage. In a previous communication he criticized other theories and said that he still believed

that compression of the central vein was the most important factor. He does not see how blocking of lymphatic drainage or the extension of edema from the brain can explain the appearance of papilledema in meningeal hemorrhages or in tumors situated in the anterior part of the orbit when there is no cerebral edema. He also points out that papilledema is never seen in compression of the optic nerve at the optic foramen or in compression of the chiasm. He believes that these two theories do not explain the frequent absence of papilledema in meningitis, particularly tuberculous meningitis. He argues that the anatomic points that have been proposed to sustain these theories are variable or inexact.

BERENS, New York.

THE PROBLEM OF THE ANATOMY OF SCHIZOPHRENIA. W. SPIELMEYER, *J. Nerv. & Ment. Dis.* **72**:241 (Sept.) 1930.

Disease of the body producing changes in the brain disturbs the cerebral anatomic picture to such a degree that all such cases must be excluded in any anatomic study of schizophrenia. Many changes ascribed to this mental disease have been found in normal brains, in those of executed persons and in soldiers who fell in the World War. Moreover, fatty substance found in glial cells and vessel walls, which have been considered as signs of pathologic disintegration in senile persons, have sometimes been found by the author in young normal persons. Many lesions hitherto ascribed to schizophrenia may have been produced by circulatory disturbances in such varying conditions as intoxications, infections, eclampsia and the epilepsies. However, the author believes that dementia praecox has correlated changes in the brain, of which he mentions a cellular loss in the third layer of the cortex, with enormous accumulation of fat and in addition active destructive phenomena in nerve tissue. In the acute stages of the disease he has found progressive and regressive changes in the glia. Because of these observations he agrees with Alzheimer and Nissl that schizophrenia is an organic disease, but does not consider that the observations suffice to establish it as an entity because such indefinite cellular losses are found in entirely different organic psychoses.

HART, Greenwich, Conn.

DISTURBANCES OF HANDWRITING IN SUBJECTS WITH ADENOID VEGETATIONS. D. J. VASILU, *Rev. d'oto-neuro-opht.* **8**:531 (July) 1930.

Agraphia is a symptom of different forms of motor or sensory aphasia and is found in other nervous diseases: multiple sclerosis, jacksonian epilepsy, dementia paralytica, etc. After discussing the mechanics and pathologic physiology of aphasia and agraphia, the author attempts to explain the disturbances in the handwriting, or partial agraphia, observed by him in school children with adenoids. In these children the writing is irregular, the letters unequal, certain letters, syllables or even words are missing, the lines are not straight, and the copy is marred by blots due to inattention. All of these faults are improved or eliminated after removal of the adenoids. When the adenoid becomes markedly hypertrophied it produces a hormone which sets up psychonervous disturbances, characterized by starting up during sleep, incontinence of urine, irascibility, etc. These same hormones may also produce excitation of a slight degree in either the graphic centers or in the coordinating cortical cells and thus produce partial agraphia. Another explanation is that these hormones may produce a vasoconstriction in the cerebral cortex in consequence of excitation of the cervical sympathetic, causing anemia of this area or of the graphic centers, which causes "amnesia in the handwriting," analogous to amnesia in spoken language.

DENNIS, Colorado Springs, Colo.

SIGNIFICANT TRANSFORMATIONS IN THE ADMINISTRATION OF CRIMINAL JUSTICE. S. GLUECK, *Ment. Hyg.* **14**:280 (April) 1930.

Considering the history of criminology since the beginning of this century, Glueck points out the rise of the humane and scientific approach to the manage-

ment of criminals that made itself felt thirty years ago, when such concepts as parole, prison work, children's courts, the self-respect of the prisoner and prevention of crime were first developed. He then demonstrates how such newer psychologic forces as mental hygiene, forensic psychiatry and the behavioristic and psychoanalytic efforts at understanding behavior have modified this legacy of criminologic point of view. He concludes with several suggestions for the future improvement of criminology. These suggestions include such plans as the assignment of the type of sentence to a scientifically trained board of psychiatrists and psychologists rather than to a judge; the use of the indeterminate sentence; the frequent psychiatric examination of defendants and convicts; the development of research and statistical work in the field of criminal psychiatry; the training of prison officials in the sociologic aspects of mental medicine; the extension of careful preventive efforts into the school and pre-school ages, and the creation of an adequately trained board concerned with rehabilitation of criminals.

DAVIDSON, Philadelphia.

CONTRIBUTIONS TO THE STUDY OF ENCEPHALITIS. G. H. MONRAD-KROHN and T. OSTREM, *Acta psychiat. et neurol.* 5:151, 1930.

The authors searched the records of the neurologic clinic of the University of Oslo for the years 1915 to 1919, that is, for the four years preceding the discovery of the first recognized case of encephalitis in Norway, to ascertain if any cases of encephalitis could be recognized retrospectively before 1919. They also compared the incidence of cases of paralysis agitans during the years from 1910 to 1912 and 1925 to 1927. They found only three fairly probable cases of encephalitis beginning in 1916 and one fairly probable one beginning in 1918; none of them could be claimed with absolute certainty as encephalitis. There had been a relative increase in the number of cases of paralysis agitans, 2.06 per cent for inpatients and 0.23 per cent for outpatients, during the three year period (1925 to 1927) over the three year period (1910 to 1912). The age of onset showed a striking difference. In the earlier period every patient was over 45 years of age, in the later more than two thirds were under 45. They surmise from their researches that the frequency of encephalitis in recent years is about as great as the frequency of paralysis agitans before the epidemic of encephalitis.

PEARSON, Philadelphia.

JUVENILE DEMENTIA PARALYTICA. W. C. MENNINGER, *J. A. M. A.* 95:1499 (Nov. 15) 1930.

William C. Menninger, Topeka, Kan., summarizes in detail the symptoms and signs in forty cases of juvenile dementia paralytica, stressing particularly the points of difference between it and dementia paralytica. He takes the position that juvenile dementia paralytica is the interaction of an immature, rapidly developing personality and a slowly progressing infection, with early distortion and later inhibition of development, and eventually breaking down of the complete biologic unit. Considered in this light, the various clinical pictures of juvenile dementia paralytica are interpreted and the differences between dementia paralytica in the child and in the adult are emphasized. Special attention is called to the cases developing in feeble-minded and often physically inferior children in whom the onset is often so insidious that it may be assumed to date from birth. Menninger takes issue with the "preparetic stage" theory, preferring to regard such asymptomatic cases as early dementia paralytica. Special consideration is given to infantilism occurring in patients with juvenile dementia paralytica, including both the physical and the mental development, with particular emphasis on the mental picture.

EDITOR'S ABSTRACT.

TUMORS OF RATHKE'S POUCH. A. AUSTREGESILLO and J. V. COLARES, *Encéphale* **25**:173 (March) 1930.

Tumors of Rathke's pouch commence to manifest their presence in the first two decades of life. This situation is opposite to that found in pituitary adenomas. Radiographic evidence of such a tumor is the suprasellar shadow corresponding to calcareous deposits. In a series of thirty-five cases histologically verified, reported by McKensil and Sosman, this suprasellar shadow was present in 70 per cent. With the exception of the two items of age and radiographic evidence, tumors of Rathke's pouch have a common symptomatology with other neoplasms of the pituitary region. Generally such tumors are formed of stratified epithelium of the pharyngeal type.

A case is cited of a woman, aged 29, who was less than 56 inches (142.2 cm.) tall, and weighed only 66 pounds (29.9 Kg.). General asthenia and psychic enfeeblement were predominant. Specifically, there was beginning optic atrophy and bitemporal hemianopia; there was also the characteristic roentgen evidence of suprasellar calcifications.

ANDERSON, Los Angeles.

TETANUS NEONATORUM. REPORT OF CASE WITH RECOVERY. EDGAR A. HINES, JR., *Am. J. Dis. Child.* **39**:560 (March) 1930.

The neurologist who is called to see a new-born child with convulsions and rigidity is reminded that tetanus neonatorum is a possible diagnosis. The disease is commoner than is supposed, the author presenting statistics to show that almost 6,000 new-born children died of this condition in the last two decades. It is due to the tetanus bacillus, and the organism is occasionally demonstrable. In spite of this undoubted etiology, the antitoxin is inefficient in the treatment for this form of tetanus. The umbilicus is the point of entry in almost all cases, although occasionally a circumcision is responsible for allowing it to develop. It is a very contagious disease and a very serious one—the mortality ranging from 95 to 98 per cent. The symptoms are those of ordinary tetanus—fever, convulsions and opisthotonos. Magnesium sulphate has been found a more effective remedy than the antitoxin, although the latter should be used. Chloral by rectum is also advised. The paper concludes with a presentation by the author of a case of his own in which recovery occurred.

DAVIDSON, Newark, N. J.

THE GROSS AND HISTOLOGICAL ANATOMY OF THE BRAIN OF A CYCLOPS. H. M. ZIMMERMAN and KONSTANTIN LÖWENBERG, *Anat. Rec.* **47**:19, 1930.

A well illustrated description of a cyclopic monster that lived for two hours is given in this article. It presented the usual malformation of the head, consisting of a single orbital cavity placed in the midline and containing one eyeball with one cornea. A rudimentary proboscis occurred in the midline above the eye. The skull was malformed to the extent that there was but a single flat anterior cranial fossa produced by a maldeveloped ethmoid bone. The brain presented an unpaired prosencephalon and a greatly dilated third ventricle. The olfactory and the optic nerves, as well as the optic chiasm, were not present. Only the fifth, sixth, seventh and ninth cranial nerves were positively identified. Histologically, the cerebral cortex was of the normal six layer type, although the individual ganglion cells were immature in development. The cellular architecture of the cerebellar cortex was that of a normal fetus of 8 months. The basal ganglia and the nuclear masses of the pons and medulla were poorly developed.

COBB, Boston.

THE MORPHOLOGY OF THE AMPHIBIAN ENDOLYMPHATIC ORGAN, W. T. DEMPSTER, *J. Morphol. & Physiol.* **50**:71 (Sept. 5) 1930.

A study of the anatomy of the endolymphatic sac and duct has been made in thirty-four species of amphibians. The histologic structure is similar throughout

the group, the sac being formed of cubical cells, which grade into the columnar cells of the duct. A part or the whole of the duct is formed of peculiar "ependyma-like" cells. The organ typically arises from the sacculus and extends to the endolymphatic foramen by which it enters the endocranial cavity. Here the saclike expansion of the organ lies in the extradural space. Six morphologic types of endolymphatic organ may be recognized in the amphibia. The development of four of these types has been followed. The structure in each case may be considered to have reached its definitive condition at the time of metamorphosis. The types of sac structure cannot be readily correlated with any habit of the animals possessing them. A discussion is given of the homology, comparative morphology and function of the organ throughout the vertebrates.

WYMAN, Boston.

THE THERAPEUTIC VALUE OF HIGH TEMPERATURE BATHS IN MULTIPLE SCLEROSIS. F. G. LINDEMULDER, *J. Nerv. & Ment. Dis.* **72**:154 (Aug.) 1930.

Being familiar with the beneficial effects of fever therapy in many organic diseases of the nervous system, Lindemulder investigated the pyrexia-producing powers of hot baths and the results of this treatment in multiple sclerosis. A dozen patients with this condition were given baths at a water temperature increased from 104 to 110 F. Immersion was carried out every second day, and each patient was in the hot water for an hour. The entire course included eleven baths. The temperature in the mouths of the patients reached a maximum of 106 or 107 F., and in one case, 108 F. Of the twelve patients, four were improved, six were unchanged and two were made worse. The author concedes that the 33 per cent incidence of improvement may be explained as representing the usual spontaneous remissions associated with disseminated sclerosis, and concludes that it is impossible to say that fever therapy by means of hot baths is of genuine value in this disease.

DAVIDSON, Newark, N. J.

TRAUMA AND DEMENTIA PARALYTICA. J. V. KLAUDER and H. C. SOLOMON, *J. A. M. A.* **96**:1 (Jan. 3) 1931.

The authors of this article discuss the following points on the subject: etiology of dementia paralytica, the onset and evolution of early dementia paralytica, trauma in determining the localization of syphilitic lesions in human syphilis, trauma in determining the localization of syphilitic lesions experimentally in rabbit syphilis, statistical studies regarding the relation of trauma to dementia paralytica, the rôle of trauma in causation of dementia paralytica, the limits of the time elapsing between the trauma and the onset of dementia paralytica which would logically incriminate trauma as playing an etiologic rôle, and the medico-legal status of the relation of the trauma to dementia paralytica. The authors urge that each case must be considered on its own merits and that the physician must try to evaluate (1) the effect of the trauma on the intracranial contents, (2) the meaning of symptoms during the intercalary period, and (3) the probable modification of the patient's usefulness and longevity.

EDITOR'S ABSTRACT.

A NEW METHOD OF REINFORCING THE ACTION OF THE OBLIQUES BY THE DOUBLE ADVANCEMENT OF THEIR SYNERGISTIC MUSCLES, EXTERNAL RECTUS, AND RECTUS INFERIOR OR SUPERIOR. L. AURAND, *Ann. d'ocul.* **167**:213 (March) 1930.

Aurand refers to the fact that Panas considered it dangerous to operate on the oblique muscles. Landolt (*L'intervention chirurgicale dans la paralysie des oculaires*, *Arch. d'opht.*, 1903) and Lagrange (*Le traitement chirurgical du strabisme paralytique*, *Arch. d'opht.*, 1903) are favorable to intervention, as are Poulard and Hartmann (*Traitement chirurgical des paralysies oculaires*, Société

d'ophtalmologie de Paris, 1923). Terrien and Lapersonne do not favor it. Fuchs considers it useless in the presence of total paralysis of the muscle. The author believes that intervention is theoretically justified in cases of paralytic strabismus in which the deviation is considerable and when marked disfiguration and persistent diplopia exist. The dizziness caused by continual diplopia is not only troublesome and dangerous, according to the degree of paralysis, but it is often a cause of incapacity. The operative technic is well illustrated.

BERENS, New York.

ECTOPIC CONE NUCLEI. A. M. CULLER and G. L. WALLS, Arch. Ophth. **3**:736 (June) 1930.

This article contains a discussion of the position of the cone nuclei in relationship to the external limiting membrane. It is usual for cone nuclei to lie inside the external limiting membrane, although occasionally some of them are seen to lie on the choroidal side. Such ectopic cone nuclei are most numerous in the central fundus, but they are absent from the fovea centralis. Rod nuclei in man are never found to be ectopic in this relationship to the membrana limitans externa. The embryologic formation of these retinal elements, and the histology of those ectopic to as well as internal to the limiting membrane are briefly mentioned. Various authorities are quoted freely in this discussion. The authors do not agree with Dimmer that the cells with the ectopic nuclei have a special function. They conclude that such cells are simply a developmental anomaly produced by a minor disturbance of the time relation between the differentiation of the cones and the formation of the true external limiting membrane.

SPAETH, Philadelphia.

THE PROJECTION OF THE MACULA ON THE AREA STRIATA IN MAN. B. BROUWER, J. f. Psychol. u. Neurol. **40**:147 (May) 1930.

Brouwer describes a case of thrombotic softening in the left occipital lobe. During life the patient had right hemianopia with preservation of central vision. Serial sections of the brain showed a small vascular lesion limited to the ventral portion of the left calcarine fissure. The external geniculate body showed evidences of a retrograde degeneration of the type which Brouwer and his co-workers had produced experimentally in monkeys. From these experimental studies and the clinico-anatomic features of this case, it is concluded that the macular projection areas in man are to be sought only in the caudal half of the calcarine region, whereas the projections of the peripheral portions of the retina are situated more ventrally. Whether the macular area in man also extends more ventrally, as it does in the monkey, the author is unable to determine from this study.

KESCHNER, New York.

PROGRESSIVE BILATERAL LESIONS OF THE MACULA IN YOUNG SUBJECTS (DISEASE OF STARGARDT). SCHIFF-WERTHEIMER and M. H. TILLÉ, Ann. d'ocul. **167**:1 (Jan.) 1930.

Tillé and Schiff-Wertheimer report two cases of progressive lesions of the macula in young subjects, and have studied the relation of these cases to progressive, familial macular degeneration (Stargardt's disease). In both cases there is a horizontally oval patch of retinochoroidal disturbance in the macular region with pigmentation. They insist that the lesions in their two cases were similar to those in the cases described by Stargardt, despite the absence of any familial history in their two cases. They conclude by stating that it seems justifiable to reserve the name of Stargardt's disease for retinal lesions of special form that affect the macula of adolescents. This condition is frequently but not necessarily familial and is slowly progressive. They doubt whether this clinical picture should be classified among retinal degenerations, but place it rather among the manifestations, in certain young subjects, of an infection the etiology of which is not always the same.

BERENS, New York.

TREATMENT OF INTERMITTENT CLAUDICATION WITH HYPERPYREXIA PRODUCED BY BATHS. H. G. MEHRTENS and P. S. POUPIRT, J. A. M. A. **95**:1910 (Dec. 20) 1930.

H. G. Mehrtens and P. S. Pouppirt, San Francisco, aver that baths which produce hyperpyrexia, because of their safety and simplicity of administration, have a field of usefulness in early cases of vascular disease with symptoms of intermittent claudication. Even in the more severe cases this therapy may find a place because sympathetic ganglionectomy, as well as the use of intravenous hypertonic saline solution, is recommended chiefly in selected cases of Buerger's disease. Arteriosclerosis with calcification is infrequently benefited by the foregoing procedures they describe, but hyperpyrexia has in the authors' experience proved worthy of trial. The milder cases offer the better chances of improvement. Cases in which gangrene has already taken place show no amelioration.

EDITOR'S ABSTRACT.

PATHOLOGY OF MALIGNANT BLADDER NEOPLASMS. H. D. CAYLOR, J. A. M. A. **95**:1736 (Dec. 6) 1930.

Harold D. Caylor, Bluffton, Ind., asserts that so-called papillomas of the urinary bladder should not be considered as benign lesions but as low grade papillary epitheliomas of the bladder, for they bear the same relationship to epitheliomas of the bladder as grade 1 squamous cell epitheliomas of the lip, for example, bear to the more malignant grades of epitheliomas in this organ. The grading of bladder epitheliomas, as devised by Broders, is described, illustrated and discussed. The importance of the removal of specimens from bladder epitheliomas as a diagnostic procedure is noted. The possibility of using diagnoses made from biopsy specimens as a basis for the development of a plan of treatment of bladder epitheliomas is emphasized and discussed. Some salient features of less common malignant lesions of the bladder are mentioned.

EDITOR'S ABSTRACT.

CONTROL OF TEARING BY BLOCKING THE NASAL GANGLION. S. L. RUSKIN, Arch. Ophth. **4**:208 (Aug.) 1930.

The tear reflex is first carefully reviewed from a histologic as well as a physiologic standpoint. The work of L. R. Mueller, which was published in 1924 (Die Lebensnerven, Berlin), is given proper credit. A composite diagrammatic drawing included in the article is descriptive. It seems as if Mueller's analysis has been given a practical clinical value. If the total amount of secretion can be diminished in cases of intractable epiphora without any danger to the eye from complete stoppage of the tears, much has been accomplished. Since the innervation of this reflex is double, in part from the cranial autonomic and in part from the sympathetic nerves, blocking the nasal ganglion (which lies in the pathway of the reflex) should decrease the secretion.

SPAETH, Philadelphia.

BISMUTH IN THE TREATMENT OF SYPHILIS. C. LEVADITI, Am. J. Syph. **14**:156 (April) 1930.

The introducer of bismuth as an antisymphilitic agent reviews the nine years that have followed since he first presented the metal, and concludes that bismuth is an efficient destroyer of spirochetes. For use in neurosyphilis, Levaditi recommends iodobismuthate of quinine. He believes that bismuth can succeed where arsenic fails, that it sterilizes the lymph glands and favorably modifies the serology. When to these virtues is added the innocuousness of this metal, Levaditi concludes that bismuth is more useful in the treatment of syphilis than any other single agent.

DAVIDSON, Newark, N. J.

THE DISTRIBUTION OF INJURY IN AMMON'S HORN. G. BODECHTEL, *Ztschr. f. d. ges. Neurol. u. Psychiat.* **123**:485, 1930.

Bodechtel reports the extent and distribution of the injury in Ammon's horn in a number of cases. There are certain vulnerable areas in Ammon's horn: Sommer's sector chiefly, then the medial curvature in the head portion, and finally the end sheaf and the fascia dentata. One area lying between Sommer's sector and the stack of the end sheaf is the most resistant of all to change. Bodechtel reports nineteen cases, profusely illustrated, demonstrating the selection of the foregoing areas in injury in Ammon's horn and confirming the previous work of Spielmeyer and Uchimura.

ALPERS, Philadelphia.

PSYCHOGENIC FACTORS IN THE ETIOLOGY OF ULCERATIVE COLITIS AND BLOODY DIARRHEA. CECIL D. MURRAY, *Am. J. M. Sc.* **180**:239 (Aug.) 1930.

Four cases are described showing a well marked time relationship between the outbreak of an emotional disturbance and the onset of symptoms. If there is a deep-seated emotional conflict and a specific organism, and if the person is predisposed in some way by heredity to pathologic conditions of the colon, the physical condition may become serious. Psychologically, in patients with colitis, besides fearfulness, there are emotional immaturity and definite childish elements. Because of these factors the necessity for psychotherapy becomes evident.

MICHAELS, Detroit.

THE EFFECT OF SPINAL ANESTHESIA ON THE CARDIAC OUTPUT. JOHN C. BURCH and TINSLEY R. HARRISON, *Arch. Surg.* **21**:330 (Aug.) 1930.

With a view to determining the effect of spinal anesthesia on cardiac output, Burch and Harrison experimented on dogs, measuring the cardiac output by the Fick technic and comparing it with a similar method after spinal anesthesia with a solution of procaine hydrochloride, 1 per cent. They discovered that a primary change occurred in arterial pressure, the average fall being 40 per cent, and that the cardiac output fell secondarily. The measured fall in minute cardiac output averaged 25 per cent.

DAVIDSON, Newark, N. J.

THE TREATMENT OF VERTIGO AND TINNITUS BY THE ELECTRO-ANESTHETIC CURRENTS OF ARAYA. G. WORMS, *Rev. d'oto-neuro-ophth.* **8**:442 (June) 1930.

This report embraces twelve cases with varied aural pathologic conditions: seven cases of otosclerosis and cicatricial otitis; two cases of otospongiosum; one case of trauma (explosion); one case of chronic suppurating otitis media and one case of tinnitus without auricular lesion. In the last five cases the treatment was without effect. In the first seven the results were: marked relief from vertigo; complete disappearance of tinnitus in three cases, improvement in three cases and no effect in one. The deafness was improved in three cases. In all cases there was an absence of an active lesion of the labyrinth.

DENNIS, Colorado Springs, Colo.

THE ACTION OF HISTAMINE ON THE INTRA-OCULAR TENSION. A. LAMACHE and J. DUBAR, *Ann. d'ocul.* **167**:133 (Feb.) 1930.

The action of histamine on the intra-ocular tension has been studied by Lamache and Dubar. In some patients intramuscular injections of from 0.25 to 0.5 cc. of histamine causes congestion of the face and a fall of intra-ocular pressure, in from one to three minutes after injection. This condition persists for fifteen minutes. Arterial tension is not changed, and the pressure in the retinal arteries is slightly raised as is the pressure of the cerebrospinal fluid.

BERENS, New York.

RETINITIS PUNCTATA ALBESCENS. L. F. APPLEMAN, Arch. Ophth. **3**:755 (June) 1930.

This article is a discussion of a typical case of the rather rare condition of retinitis punctata albescens. It is a congenital defect of the highly specialized nerve tissue which constitutes the retina. There are: an absence of inflammatory changes, a marked bilateral symmetrical similarity, a stationary night blindness which dates from early life and is probably congenital and a multitude of white spots in the retina not accompanied by any pigmentary changes nor by a progressive impairment of vision — factors pointing to a probable congenital development of the disease.

SPAETH, Philadelphia.

MANIC-DEPRESSIVE PSYCHOSIS IN IDENTICAL TWINS. ISABEL BRADLEY, Am. J. Psychiat. **9**:1061 (May) 1930.

Calling attention to the opportunity for investigation of the relative influence of heredity and environment offered by the study of personality traits in twins, Bradley presents an appropriate case. Her patients were identical twins; in one a manic-depressive psychosis developed at the age of 32, in the other the first attack occurred five years later. Bradley believes that this case and others like it support the hypothesis that mental disease is dependent on hereditary defect in the germ plasm.

DAVIDSON, Newark, N. J.

POLIOMYELITICIDAL ACTION OF NORMAL HUMAN SERUM. CURRENT COMMENT. J. A. M. A. **95**:1269 (Oct. 25) 1930.

The recent work of Shaughnessy, Harmon and Gordon has shown that normal serum of persons over 2 years of age is much more effective in combating poliomyelitis virus in vitro than is convalescent serum. More important, they have shown that there is feeble combative effect in serums of children under 2 as compared with those over 2 years of age, a condition similar to that in diphtheria immunization.

CHAMBERS, Syracuse, N. Y.

OPTIC NEURITIS COMPLICATING PREGNANCY. A. PATRY, Ann. d'ocul. **167**:14 (Jan.) 1930.

A case of unilateral optic atrophy with sharply delimited bitemporal hemianopia, without other local or general disturbances, is reported by Patry as a complication of pregnancy. Ten similar cases observed by other authors are also reported. He concludes that the clinical picture is due to compression of the nerve by the hypertrophied pituitary gland. The prognosis in cases of these lesions is grave, as they lead either to blindness or sterility. Active treatment consists in preventing or interrupting pregnancy.

BERENS, New York.

TREATMENT OF PERNICIOUS ANEMIA WITH DESICCATED, DEFATTED STOMACH. CYRUS C. STURGIS and RAPHAEL ISAACS, Am. J. M. Sc. **180**:596 (Nov.) 1930.

In twenty-two patients with pernicious anemia, desiccated defatted hog stomach given in dried form in daily doses of from 15 to 40 Gm. produced definite hematopoietic remissions. The average count at the beginning of the treatment was 1,800,000 red blood cells per cubic millimeter, and the average count at the end of 6.6 weeks was 4,300,000. Further experiments suggest that the hematopoietically active substance is not present in the layer of muscle, but probably some of it is present in the mucosa.

MICHAELS, Detroit.

## Society Transactions

### NEW YORK ACADEMY OF MEDICINE, SECTION OF NEUROLOGY AND PSYCHIATRY

*Regular Meeting, Oct. 14, 1930*

MICHAEL OSNATO, M.D., *Chairman, in the Chair*

#### SOME PRINCIPLES IN THE TREATMENT OF BEHAVIOR PROBLEMS IN CHILDREN. DR. LAWSON G. LOWREY.

In attempting to treat children with behavior problems one has to care for present behavior problems and to prevent the development of more serious problems in the future. They may, in general, be classed into two groups: the direct and the indirect. Direct measures comprise those in which the physician and his assistants deal directly with the patient. They include any necessary physical treatment and psychotherapeutic measures of any sort which represent direct work with the patient. In the indirect group would be classified social-manipulative measures intended to convert the environment of the child into a source of positive rather than of negative stimuli.

It is not easy to determine the types of cases best suited to the two methods of approach, for one is treating a situation or a series of situations involving individual and surroundings. The child is a complicated personality at whatever stage of development he may be in age, general development and experiences, living in a variety of groups. There is the home setting, the neighborhood and neighborhood companions, the school setting, if the child is of school age, etc. Each of these presents dynamic features which stimulate behavior, either positively or negatively, in the direction in which personality is evolving. Negative stimuli mean that the environment is so organized, or disorganized, that the series of stimuli presented tend to disorganize the personality, while the environment may be said to be positively organized when the general trend of the stimuli arising from it makes for a wholesome personality with the minimum amount of objectionable behavior.

In manipulating environments, measures may be divided into two major groups: (1) The manipulation of things, as, for example, the school, so that the child has a more adequate placement in the light of his abilities. Thus, he may be a motor learner; he may fail in the regular grades but in vocational school may be successful and may become both a more harmonious personality and a harmonious reactor in his social setting. There are several points needed for the development of an organized personality. First, the satisfaction of a feeling of achievement—the child's, not that of some one else. As a corollary to that, he needs recognition from people that he is an individual who is of value in various ways. The child who is placed in a grade in school in which he is constantly failing to achieve a feeling of satisfaction in his work and recognition from the group is thwarted and may develop various abnormal symptoms. To place the child in a setting in which these things may be achieved becomes, therefore, an important measure in his treatment.

Again, each individual needs an affectional relationship with other persons. Frequently, children are deprived of this, or the affection shown does not meet the needs of the child. Treatment here brings one into contact with a host of the subtler undercurrents of the minor phenomena of everyday life. Older children of a family group frequently feel that there is discrimination in the way the children are treated. They may feel that they have a hard time and that the younger children receive all the affection, recognition and privileges. In some degree, a jealousy reaction is fairly common in the older children of a family, sometimes to the surprise of the parents. Springing from the little things of everyday life,

these reactions may be difficult to interpret, but, after all, it is what the individual feels or believes that counts.

Another thing that the individual needs is a feeling of belonging to a group in a different sense from that of achieving recognition from the group. It is the feeling of security as a member of the group that is valuable here.

The manipulation of things becomes very much mixed with the problems of manipulating people. Changing the child's neighborhood, introducing him to recreational groups, altering his position in school, utilizing the summer camp, helping the family with financial aid and many other concrete steps may be taken. In the last analysis, most of the success in treatment that occurs, does so because the individuals concerned are able to work out their problems. Change to a new neighborhood is important in the change of companions and play. Change in the school system or a change of curriculum may be enough, but there must also be wise management of the child's problem by the teachers. The summer camp brings to bear another type of group influence.

The manipulation of people is the second type of indirect approach. Within the home by far the most important factors are the people and their attitudes. Perhaps the most important of these is the mother. If there are intricate problems connected with the home, one may have to use intensive psychotherapy with the mother or some other important member of the family.

My colleagues and I have recently worked out a new, simple, fivefold classification of the common groups of the factors involved in the causes of behavior disorders, which is important in focusing treatment. The first groups include the conditions that are most grossly pathologic, most easily diagnosed and in which routine treatment is best established. Group I, the gross mental deviations, includes the psychoses, ordinarily in mild form, most commonly called prepsychoses, feeble-mindedness and epilepsy and, for want of a better place to put them, the behavior disorders following epidemic encephalitis. Group II, the gross physical deviations, is highly important because the treatment is in considerable part determined by what must and can be done with reference to the physical disability, yet it must help the patient to meet the psychologic situation with which he is faced. Group III, the neuroses, demands in the child, as in adults, intensive and special therapy to stabilize the personality. Clearly these three groups demand expert treatment and individual attention if much is to be done to alleviate or help the conditions. Group IV, the complexes and conflicts of less than neurotic level, represents the common meeting-ground of different technics and the battle-ground of a variety of professional groups. It shades off on the one side to the neuroses and on the other, to group V, presumably the simplest group of problems, represented by ignorance or faulty training. The lack of knowledge of child psychology or proper training methods results in a variety of difficulties. It is here presumably that work in child training and parental education proceed with the greatest profit to everyone. There are some difficulties, however, as in many cases the lack of information or the ignorance of the parents depends not so much on an intellectual difficulty (even occurring despite the fact that the parent has knowledge) as on the emotional conflicts of the parents themselves. At this point there is a need to reinforce parental education and methods of child training with the type of clinical work that is designed to assist in breaking down these conflicts and complexes that prevent the individual from putting knowledge into effect.

One can, then, say of the first three groups, that expert treatment is demanded. In the fourth and fifth groups, a variety of technics come together. It is primarily in these groups that sociologists have been saying that they have found the answers; that psychologists have sometimes said the same; that educators believe that they hold the necessary answers to what should be done, and so on. So many types of clinics represent this overlapping of technics. I should like to repeat that the answer is simple. No one group has all of the answers to the problems of human behavior, and the greatest profit is derived from a joint and unified attack.

Sometimes in an intense interest in the conflicts and attitudes which underlie behavior disorders, one may disregard simpler, more direct, more accessible socially

manipulative measures or an intellectual approach to the problem of the relationship between the child and the parent, and having neglected them, one may suddenly find a complicated situation on one's hands, which cannot be handled under clinical conditions.

As experience has amply demonstrated, at least to me, it is best to begin with the simplest and the most direct measures that will affect the situation. It is important to utilize these first and then to proceed into the complicated emotional tangles only so far and so fast as is necessary. In this type of treatment, as in any form of psychotherapy, it is found that it is much more dangerous to proceed too rapidly than too slowly. If progress is too rapid, things are precipitated before one is ready for them. Proceeding more slowly, there is time for understanding and insight to develop, as well as that confidential rapport that is so highly important and even more necessary with the child than with the adult. Often, in attempting to analyze the causes of success in treatment, it would appear that the most important point involved was the relationship established between therapist and patient, in which the therapist came to be highly valued by the child. Very often in talking over his problems, the patient succeeds in clearing up emotional conflicts in a fashion acceptable to him and to others, without gaining a deep insight into them. It is often necessary to try to ascertain what the early experiences of the parents have been and how these might be modified. It is precisely here that it is important to remember that the jump from the present situation to the early genetic history of the parents is a long one, with many steps to be taken in between.

A general outline for the program of treatment might be the following: In early childhood, the most important points seem to lie in the parents' handling of the situation, therefore, the treatment approach is largely indirect. During the school age and part of adolescence, the direct and indirect methods of approach are about equally needed. In adolescence, particularly in late adolescence, the direct approach is most necessary. In any case, the attempt must be focused on stabilizing the child in relationship to himself and to the totality of his environment.

#### MATERNAL OVERPROTECTION AND REJECTION. DR. DAVID M. LEVY.

An analysis of maternal overprotection was made by selecting from large numbers of overprotected children, twenty cases in which the overprotection was obvious—pointed out both by lay observers and professional workers—and in which the patient was clearly a wanted child. The object was to select cases of this human relationship in its simplest and most complete form; then, to think through all the significant facts known about the parents and children involved in the relationship in the terms of this study. In contrast with other cases of maternal overprotection, the twenty selected for this special investigation were referred to as "pure" forms.

The term "maternal overprotection" was accepted as synonymous with excessive maternal care of children. It connotes such terms as babying, oversolicitude, too much mothering, overindulging and a host of similar expressions indicating that the mother exceeds the "normal" in her care of the child. According to our clinical observations, the excess may be formulated in terms of: (1) excessive contact, e.g., a mother sleeping with her son, aged 14; (2) prolongation of infantile care, e.g., breast feeding to the age of 4 years; (3) prevention of the development of independent behavior, including such descriptive terms about the mother-child relationship as, "she won't take any risks," "she always fights his battles," and (4) lack or excess of maternal control, shown in overindulgence of the child in regard to privileges or possessions, and by the child's disregard of eating and sleeping time—in general, by his doing what he pleases undeterred by the mother's commands or pleadings. This is in contrast with excessive maternal control in which a relative overmodification of infantile traits is manifested in undue obedience on the part of the child.

All factual data on maternal overprotection, when formulated by this plan, show much dovetailing; nevertheless, the stress is often found greater in one group than in another. It appears so far that overindulgent overprotection yields aggressive-egocentric behavior of varying degrees in the offspring, whereas dominating overprotection yields submissive and effeminate behavior. Since in our cases the patterns of the mother-child relationship appear to have been well established in infancy and by a series of factors operating in the mother before the birth of the child, the mother-child relationship is considered primary; all other factors (the patient's relationship with other adults and children, physical and intellectual factors, and special abilities and disabilities) as secondary modifying influences, exaggerating or diminishing the influence of the primary relationship. For example, consider the case of a child who is treated by his mother more like a baby, is held closer to her and is more dependent on her for aid in his school work and in social contacts than are other boys. At 7½ years, he is referred to the Institute for Child Guidance for symptoms of irresponsible, dependent and immature behavior in keeping with the overprotective relationship. He presents a series of submissive and aggressive traits, though largely the former. His teachers note his docility. He accepts the lead of his brother, aged 4, in play, and likes to indulge in baby talk. This docility is in contrast with his wish to dominate the group, yet he runs to the mother for protection from other boys. Although in the primary relationship such observations are easily discerned and anticipated, yet they are influenced considerably by the following factors in this patient: developmental delay and inadequacy of muscular strength, coordination and intelligence. Besides these factors, there are an interfering, indulgent grandmother, a father who favors the younger brother and a great deal of rivalry between the brothers. In this case, as in all others of "pure" form, the events following infancy affect, as in this case they intensified, an overprotective relationship previously established.

After classifying the symptoms of overprotection as they are objectively manifested in the mother-child relationship and through the behavior pattern of the child as its direct outgrowth, all factors in our social-psychiatric investigation are evaluated in terms of the primary relationship in the following order:

1. Period of anticipation during pregnancy and childbirth of patient. All conditions that delay the coming of a wanted child in the form of relative sterility, miscarriages or stillbirths obviously compel the mother to go through periods of anticipation and frustration. The maternal attitude toward the child, following such experiences, will be more apprehensive and protective than if the child's birth occurred in the usual time. Such experiences occurred in our series eight times.

2. Extra hazard. The illnesses of infancy and childhood were evaluated in terms not of their actual seriousness but of the maternal response. It was found that frightening illnesses or accidents in which the child "looked dead," as in fainting and convulsions, from whatever cause, stimulated more overprotective response than familiarly known though serious diseases. Protective and infantilizing care and prevention of the usual training of children may be occasioned, for example, by frequent "colds" and operative procedures, as well as by actual deformity. An only child or a first child, who, however long, is an only child, represents a greater risk than a child who is one of a large family. If it is known or assumed by the parents that an only child represents, or is, an only pregnancy, the hazard is presumably increased. A combination of events such as a relative sterility or a succession of miscarriages, followed by a viable child, after which pregnancy is considered impossible, is a frequent pattern in our series.

3. Maternal factors. Satisfactory sexual and social life with the husband sets up a number of conditions that operate against a mother-child monopoly. On the other hand, sexual incompatibility and lack of social interests in common with the husband intensify the mother-child relationship. The child must then bear the brunt of the unsatisfied love life of the overprotective mother and absorb

all her social activities. Such observations are especially frequent in our group. Sexual incompatibility occurs in every case.

In the early life of the overprotective mothers, two factors stand out clearly: inadequate affection and early responsibility. The responsibility is shown in early self-support or contribution to family earnings, and also in occupying an authoritative position over other siblings. It appears plausible that mothers in our group, affection-hungry since early years, try to satisfy their incomplete lives almost exclusively in their maternal relations. Attaining that state, they intrench themselves in a mother-child monopoly through an aggressive offensive against all intruders, including the husband, who, frequently submissive to the wife, may not interfere at all in matters pertaining to the child and who frequently is not consulted. The wife is competent, takes responsibility readily and is often derogatory of her husband. Such observations apply to fourteen mothers in our series. In the remaining six, the overprotection is of the submissive, dependent type—mothers who, divested of other social relationships, cling to the child as though in a hostile environment. Such mothers are in contrast with the larger group of aggressively overprotective mothers. The picture of the latter group is that of mothers, independent and competent, who, attaining their love-object in an offspring, push away everyone in the effort to create a mother-child monopoly. In the case of the dependent, overprotective mother, the situation is reversed, though with a similar result. She is in a passive relationship with the social environment—the mother-child monopoly is created for her.

4. Paternal factors. The following characterization of the fathers is consistent in our series: responsible, steady workers, submissive to their wives, dependent on them for family decisions, who exert little influence on the patient or add to the overprotection. The fathers in our series do not exert authority in the family, are not looked up to by the wife for family decisions, or do not aid in disciplining the child; hence, they do not help in mitigating the effects of the maternal overprotection. When the paternal rôle is weak or negligent, the maternal rôle is unmodified. Given an inadequate or indifferent father, it is assumed that, out of necessity, the mother plays a more important rôle with her child. This holds true especially in cases in which no paternal influence exists, as in the case of widows or divorcees.

5. Other factors modifying overprotection. Of these factors, relatives chiefly were considered. Some cases, as in our series, are complicated by a grandmother who lives in the home and whose rivalry with the mother is manifested in an overprotective attitude toward the grandchild.

6. Problems of the patient. General attitudes of our patients may be classified according to behavior manifestations, as aggressive, submissive or indifferent. All of these forms may be represented in any given case. Aggressive behavior, however, is the most frequent of all of the forms, and also most readily understood as an expression of the dynamics of the mother-child relationship. The child's attempt to dominate every situation, and its corollary, his refusal to yield to other persons, results in a series of complaints from teachers and parents that are well comprehended under the heading, "rebellion against authority." This includes various forms of disobedience, impudence, temper tantrums, bullying and general undisciplined behavior. The freedom of action and speech which parents allow these children is often extreme. In a number of cases the point of tolerance of the parents toward the child is reached. The typical attitude of the mother toward such a child is that, as a reward for all her devotion, she has reared a monster who makes life intolerable for herself and her husband.

The irresponsible behavior of both the submissive and aggressive child is explained on the basis of unmodified and overmodified infantile experiences. In the aggressive child, it is understood as a throwing off of responsibility, a refusal to do one's share; in the submissive child, as an immaturity, an infantile expectation of help from others.

Consistent for all of these patients is the difficulty in making friends. The most frequent reason for this is the attempt on the patient's part always to be

leader, to boss the game, to give orders, to quarrel and to fight. A small number keep away from friends because of timidity or refusal to join in rough sports. A number of patients have been entirely restricted to adult society until school age; a number have not been allowed to play with other children in the neighborhood.

Difficulty in making friends is understood as a carry-over of the mother-child monopoly. The inability to make friends reinforces maternal overprotection. It compels the mother to bear the brunt of the child's unpopularity. With the absence of friends, an important mitigating influence of maternal overprotection is lost. The group of boys, so far as it puts a value on independence and courage, is an antidote to infantilization. It strikes out against mother dependency. For our patients, the value of the group in developing freedom from maternal overprotection is lost.

When difficulties occur in the classroom they follow closely the overprotective pattern, mostly in the form of attention-getting behavior. Our patients for the most part, however, are good students, a few of them excellent. School work, as well as secondary interests (evaluated in terms of maternal overprotection), are seen as helpful agents in the development of "independent" success on the part of the child. Failure in school throws a further burden on the mother-child relationship. The excellent adaptation to the classroom on the part of some of our patients is explained in terms of satisfaction through achievement, made easy by natural abilities; in some cases, when it is consistent, it is response to the authority of the school teacher, and for the most part, it is an identification with the educational values of the mother. It has been shown that for certain objectives, overprotective mothers sacrifice all their indulgences and become stern, unyielding and effective. The child then learns to surrender when all the artifices, used successfully in eluding most responsibilities, fail.

Of the "vegetative" adaptations, our patients show more frequent bladder control than the general group, though more feeding problems. This is consistent with the careful bladder training by the overprotective mother, in contrast with that by the negligent mother who has a correspondingly greater number of problems in this regard. The acts of eating and sleeping become socialized through excessive contact with the mother, and hence, more frequently a difficulty.

Developmental data show nothing significant in regard to motor or speech development that is not consistent with the intelligence of the children.

Overprotected children in this series average nine months on the breast, in contrast with children of rejecting mothers, who average four months on the breast.

Check groups for this study have been made on 200 other cases at the Institute, taken seriatim from the records, weeding out the overprotective cases. The frequency of sexual incompatability was compared with normal samplings and with other groups.

#### DISCUSSION

DR. H. E. HAWKES: In Dr. Lowrey's presentation, I was particularly impressed with the fact that the methods which he mentioned and the kind of problems he discussed were almost exactly of the same kind that I meet every day in my office. I deal with college boys, or men as they like to call themselves, between the ages of 16 and 22. I am responsible for the discipline, what little there is, in a college of 2,000 boys; in my office the entire personnel dealing with these boys outside the classroom heads up. In fact, the long case report that Dr. Levy read in the latter part of his paper presents some aspects that sound very natural to me.

I see many parents and they are not pests to me, at any rate not always. In my experience there is one aspect of a parent, however, that is more common than any other—precisely that mentioned in these papers. Apparently the most difficult thing for parents to learn is the fact that they brought into the world another and an independent life; that this child, this boy, is no longer attached to them; that he is no longer one of the members of the father or the mother. It is hard for many parents to forget that they have brought into the world an

independent being. Occupying a high middle ground between father and mother, as I do, when they call at my office I frequently have to tell them—usually the mother—that this boy did not ask to be born, that he had nothing to do with it, that he is just as independent a personality as they are, and that it is high time they began to treat him as such.

As far as I can see, the differences between the normal and the abnormal are not very great. My grandmother, a mild old lady, when everyone would be sitting around criticizing the neighbors, used to say, after they had handed out a particularly vicious criticism, "Well, there is enough about us all to spoil us." There is something abnormal about us all, but we hope that the center of gravity is normal.

Another thing that Dr. Lowrey mentioned interested me because of the way in which it fits into my work. This has to do with the way boys have to be approached. He said that the most important thing he had to present was the fact that one ought to start with the simplest aspect of a situation. This is just as true in dealing with the normal as with the abnormal person. One of the principles that it took me years to learn, but which is very simple to state, is that in approaching any question one must start from where he is. I acquired that principle from a story of a traveler who asked a Welshman, in Wales, the best way to get to Canarvon. They were a long way from the town, and it was over the mountain. The Welshman, after a moment's thought, said, "Well, sir, I would advise you not to start for Canarvon from here." There are so many people, not only in your business but in mine, who want to start from some other place than that in which they are. One cannot do that. One must start from the spot in which he is and work with the things in sight, the things at hand.

In my office I have to remember sometimes that a college must not be treated like a sanatorium. It is not supposed to be a sanatorium. It is supposed to be a college, which has certain elements of difference from a sanatorium. At the same time, there are boys, several of them each year, who show symptoms that should be recognized. I do not know a thing about psychiatry; I wish that this were not the case, but it is true. My handling of these cases is not very professional, but it is the best that I can do. I ask the instructors to let me know when they suspect that there is something the matter with a boy. Then I see the boy. The reputation of my office is such that there is no feeling of disgrace in there. The boy is not ashamed to be seen there, and does not become upset. There is a university physician who has access to psychiatrists if their services are needed. How to provide contact between the boy and the physician is the principal question. The boy comes in, sits down and we begin to talk about something or other. I tell him that he is not looking well, that perhaps his digestion is out of kilter. (I find that the autobiographic method always helps.) I tell him that mine was out of kilter once and I found it a simple matter to get it fixed up; that I was getting a lot of poisons into my system, and that probably he is too; that I can tell by looking at his face. I advise him to see the university physician. He starts out, and while he is on the way I telephone to the physician and tell him who is coming so that he can be ready.

I know that in Columbia College we ought to have psychiatric advice suited to our local situation, and that those of us who are working with the individual student ought to be better informed than we are about the earmarks of mental unbalance and disease. We need someone to tell us what to look for, so that we can recognize the abnormal cases earlier and more intelligently than we do. I hope that some method for doing that can be worked out.

The greatest difficulty is in distinguishing between normal immaturity and an abnormal condition. It is not always easy for one to tell the difference between the actions of a boy who is simply mischievous and one who shows signs of abnormality that ought to be looked into. Most of this sort of thing comes to my office in terms of discipline. The principles on which discipline is handled nowadays by sensible people, that is, by people who agree with me in the matter, are utterly different from the way in which college discipline was handled only a few years ago. Discipline is not a question of a rule and a penalty.

When a boy is admitted to college, one assumes that he has good intelligence. One can find that out, and I do. Through the medium of a good physical examination I determine the state of his health. I try to find out whether he has a good character. We admit him, and having done so, undertake a responsibility to educate that boy in mind, body and soul. The very moment that we find that he is not perfect in mind, we do not dismiss him, we try to teach him something. When we find that he is not perfectly developed physically, we do not put him out; we help him to try to correct the defects and to build up a body that is useful and satisfactory. In the same way, when we find a boy not perfect in character we ought to do something about it. The department of admissions may make and does make mistakes. We sometimes have a boy who does not know anything, and in such a case he has to go. We may find a boy not up to the level in the development of character which we assume as the minimum, and we let him go, but not the first time that he shows a tendency to error. In this way discipline is a constructive phase in character building, as the curriculum is a constructive phase on the intellectual side. I cannot go into detail in regard to the way in which this is worked out, I can merely state the fact. I also state the fact that every officer of discipline in our personnel has a tremendous amount to learn from those of you who are treating the abnormal, and perhaps you have something to learn from us, provided we do our jobs as carefully as you do yours.

DR. G. S. AMSDEN: One of the great difficulties confronting many physicians who deal with children, and probably also with college students, is that the child does not come to the physician as the adult does, but is brought. The situation is entirely different. One cannot depend on the child for the spontaneous cooperation that the adult brings. Then again, there are other difficulties, namely, that the physician is apt not to try to grasp and understand the child in his own terms. The child is far more knowing, far more penetrating in his judgments and understanding of his environment than we adults are prone to believe. The difficulty is that the terms in which this understanding is couched are totally different in the child than in the adult. The physician who deals with the child must have a personality which is suitable, which adapts itself well to this problem.

Dr. Lowrey spoke about the speed with which progress in dealing with the patient goes ahead. The results cannot be judged. Little can be said about the result from the speed with which the physician gets on with his patient. We have long since learned that mere explanation, even so far as adults are concerned, is far from adequate. It is easy to explain to adults mechanisms and difficulties in terms which to the physician seem clear to be understood and to carry effect; but one finds that that is not so. One has to give the adult patient rope and let him do a good deal of finding out for himself. The part the physician plays is that of somewhat skilfully playing out the rope and pulling it in again. With children this is a far more delicate and difficult problem. The child must be allowed to develop his difficulties for the physician in his own way, and the physician must be prepared frequently not to understand his patient for a long time. So, little can be said by way of adverse criticism of the slowness with which progress is made in dealing with children.

Another important point is this. The physician, in more cases than one is apt to suspect, acquires an extraordinary rôle in the eyes of the patient. The child comes from an environment such as Dr. Lowrey has elaborated; the difficulties are manifold, and more often than not the physician soon comes to represent to the child the embodiment of all of these difficulties. His problem in dealing with the child is therefore an exceedingly delicate one. He must proceed with slight explanation. He must lead the child, so to speak, to the blackboard to find what is written on it, and prepare him to understand it in his own way. This requires infinite patience and a prolonged period. If done successfully, as Dr. Lowrey has illustrated in so many instances, at the end of a long time remarkable results are secured. Then comes a further situation. The physician has by this time won an important position in the eyes of the patient. The next

problem is that of disentangling the patient from the physician in such a way as to gain for him an independence of the physician, so that he may leave the physician with the secure feeling that he can paddle his own canoe.

DR. EDITH R. SPAULDING: One of the most discouraging aspects of the treatment of conduct disorders is the fact that the personality deviation in the child is often based on a much more deeply seated personality deviation or mental abnormality in the parent or parents. It is the child, however, who is brought for treatment, frequently, as Dr. Levy pointed out, with reluctance on the parents' part and often only because of a teacher's insistence. One's hands are often tied when it comes to the treatment of the parental situation. Although the need for treatment of the parent may be greater than that of the child, it often cannot be undertaken directly. Dr. Lowrey's solution of dealing with the situation through what may seem a somewhat superficial treatment of immediate conditions is probably the wisest procedure known at present.

The classification of treatment that Dr. Lowrey outlined serves to emphasize what would seem to be the most urgent problem in mental medicine at the present time, namely, the therapy or mental dosage that is best suited to different types of cases. When to interfere with mental mechanisms (if one may use the term interference as it is employed in the obstetrical field), how to interfere and to what extent to interfere, are questions that may well receive more study in the field of mental and nervous disease in general, as well as in that of conduct disorders. The same fundamental principles are to be found in both fields.

The first requisite of proper mental dosage in psychiatric conditions in general is perhaps the realization that abnormal emotional states and even the conversion symptoms of hysteria are just as real to the patient as any symptoms caused by physical pathology, and that before the abnormal mental state or conversion symptom has developed the patient has passed through mental experiences usually associated with actual suffering that are as definite in their sequence and causality as the stages associated with an infectious process. This may be equally true in behavior problems.

The second requisite, after a diagnosis of the condition has been made and the underlying mechanisms are understood as well as is possible, is the appreciation of the fact that mental procedure may be as definitely planned and as systematically carried out as though the case were being treated from a physical point of view. It may be said that physical therapy varies greatly in the hands of different physicians, or that there are actually as many therapeutic credos as there are physicians. While this is true in the superficial adjustment of treatment, it is also true that there are well recognized principles underlying physical therapy which point the way to the technic selected.

In cases of inoperable cancer the patient is made as comfortable as possible and only palliative measures are employed. The patient is often not told the seriousness of the situation. This is not unlike the treatment of a deteriorated schizophrenic patient in whom the process has advanced too far for much help. He is made as happy as possible within his limitations and little attempt is made to work with his emotional conflicts or to give him insight into his mental condition. In cases of early cancer the physician is called on to work quickly and intensively to eradicate the disease process. This is also true of the incipient stages of schizophrenia.

As the rôle of prevention of cancer assumes more and more an important place in the eradication or lessening of the disease, so the rôle of prevention in mental disease is steadily increasing.

In pneumonia and in tuberculosis, supportive treatment is given to raise the bodily resistance. That in general may be said to correspond to the treatment of a depressed person who is encouraged and given suitable occupation and protection, but whose deeper or unconscious mechanisms are not interfered with until he has recovered sufficiently to be equal to it.

In the mental dosage given to psychoneurotic persons, choice must be made between different types of procedure. Some patients will be greatly helped by

reassurance and suggestion or by new occupation; for others, such treatment will be entirely inadequate. Some will be cured almost miraculously by hypnosis; others will be made worse. Some will be cured only by prolonged psychoanalytic treatment; with others this may prove ineffective. It is probably true that in many cases in which psychoanalysis has proved of little help, the fault has been in the unwise choice of the case submitted to that type of treatment, rather than in faulty psychoanalytic technic.

Here again, the bringing to consciousness of that part of the patient's life drama that has been unconscious is a delicate process. It must be handled with much more care and judgment than is used in the administration of strychnine, of mild mercuric chloride and of morphine. One must study the tolerance of the patient at each visit and give him only the dosage he can stand.

Better results will be obtained if one chooses the type of therapy best suited to the individual patient instead of trying to fit all patients into the same therapeutic mold. The types of cases described by Dr. Lowrey demonstrate the difficulties of such a choice and the importance in certain instances of not interfering too much. Statistics show that infant mortality in certain countries is higher in the practice of physicians than among midwives. This is accounted for by the lack of interference among the latter. On the other hand, to treat a suicidal patient with passive measures and not to interfere at once and protect him from the possibility of self injury might easily prove disastrous.

Medicine has always been classed as an art. The mental side of it especially calls for an artistic approach. But art is based on as definite principles as is science. Leonardo da Vinci used to say to his pupils, "Be as careful of the light in your picture as you would be of a rare jewel." Does this not express, perhaps, the desirable attitude of the physician toward the emotional state of his patient, that is, the delicacy and skill with which mental dosage should be applied.

The papers of Dr. Lowrey and Dr. Levy have, I believe been most helpful in showing important underlying mental and environmental causes in certain types of cases, and in suggesting a valuable use of psychiatric light and shade in the composition of therapeutic paintings.

DR. SANGER BROWN, II: It is not possible to listen to these excellent papers without having it impressed on one that society has not done what it might for children, especially those showing abnormalities of conduct or behavior disorders. One must remember as one goes back into the history of society that frequently not as much has been done for children as might have been. Child abandonment, it is true, is not very common now; but it is not long since there were difficult problems of child labor. Education of the child was neglected, and was not enforced until such people as Horace Mann, not over a hundred years ago, made it compulsory. Discipline of the child used to be handled by the courts, and in England it was not unusual for a child to be sentenced to seven years in prison. Things like this make one feel that while parents may be solicitous for their children, society as a whole has not done very well by them. In the field of social care that Dr. Lowrey and Dr. Levy have presented, there are to be seen gaps in our management of these problems. A number of interesting things are developing at the present time which will, I think, fill in these gaps. One is parental education, as given in such colleges as Columbia, Rochester and Vassar. Nursery classes are being formed at these colleges and parents taught the rudiments of habit formation and the early training of children. Another activity is the spread of kindergartens. It has been said that the child properly trained in kindergarten never makes a bad man. This may be an overstatement; nevertheless, the training received in these early years is invaluable.

Dr. Lowrey spoke of vocational and manual education for children. This is an important movement; when developed in the schools as it should be, it is probable that many problems will disappear. A child can be taught in these ways when he cannot learn from books.

A scientific attitude toward children's problems is beginning to develop in the children's courts, children's institutions, and agencies for the care of children.

I think that this will have an important effect on the prevention of the types of disorders discussed here.

I thoroughly concur with Dr. Lowrey that once a case is established, the treatment that it should have can well be compared with that for acute tuberculosis. It is a case for a specialist. It is as dangerous to treat such a condition unscientifically as to treat a case of tuberculosis by casual means.

DR. LAWSON G. LOWREY: There is one point in what Dean Hawkes said that I should like to emphasize. I see no borderline between the mentally normal and the mentally abnormal, and I have never been able to find any specific varieties of general social behavior which can be said to be genuinely indicative of abnormal mentality. We have neurotic, feeble-minded and epileptic children whose behavior manifestations cannot be told apart. What tells the final story is analysis of the entire situation and the different factors leading to the behavior. Some of the behavior of intellectually highly gifted persons, is in general as foolish and unmotivated from the social point of view as that of the feeble-minded. Again, I certainly agree with Dean Hawkes that a college is not a sanatorium. This is an important point that some colleges are having difficulty in recognizing. The modern clinic for child guidance is not exactly a sanatorium either, because the vast majority of people coming to it would be rated as normal, and the vast majority of children studied belong in the same group.

I would make one comment on Dr. Brown's remarks. It is true that many movements are under way, some of a clinical nature. The great difficulties at present are the coordination of facilities, the avoidance of useless and unnecessary overlapping in these fields, and the extension of facilities until a larger and larger group is reached. As I see the general situation, it is unlikely that actual clinics for mental hygiene will exist in the next fifty years to take care of the manifold problems that arise. I believe that constructive prevention is better than therapeutic prevention. I think that our job is to coordinate our clinical observations, so that they will be more useful to larger groups of people, in terms of preparental and parental education; in other words, to surround the child from the beginning with the constructive type of environment and stimuli that will lead to the evolution of the kind of personality one wants to evolve, rather than to try and correct it when minor problems develop.

#### PHILADELPHIA NEUROLOGICAL SOCIETY

*Regular Meeting, Oct. 24, 1930*

WILLIAMS B. CADWALADER, M.D., *President, in the Chair*

#### COMPRESSION OF THE SPINAL CORD BY A FIBROBLASTOMA SUCCESSFULLY REMOVED. DR. ALFRED GORDON.

A woman, aged 54, with a good antecedent history, had begun to complain of pain in the lower part of the back seven years before presentation. At times the pain was sharp, and during these periods the patient was treated for chronic rheumatism, for uterine displacement, for supposed adhesions, for sciatica and for diseased tonsils and teeth. Soon after the onset, she began to have pain in the left leg and weakness in the right leg. This pain continued progressively. The patient came under my observation in June, 1930. At that time physical examination showed a flaccid paralysis with foot-drop of the right lower extremity; knee jerk absent on the right and much diminished on the left; no ankle clonus; the plantar reflex, flexor on the left but indifferent on the right, and the abdominal reflexes, normal. Objective sensation for pain and temperature was markedly diminished and in some areas abolished—in the left leg, from the knee down and also partly in the lower portion of the left thigh. Touch was normal. The right leg presented no sensory disturbances. Pain was present chiefly in the lumbosacral region and in the left leg, but occasionally also in the right leg. The

pain had a radicular distribution; it was particularly severe on coughing or bending forward. There was also numbness in the left leg. There were no objective sensory disturbances over the perineum, abdomen or lumbosacral region. The entire right lower extremity and the gluteal region on the same side showed considerable atrophy. Two bedsores were seen. The sphincters were involved. There was no protrusion of the spinous processes, but the twelfth thoracic and the first lumbar vertebrae were tender to pressure. Roentgen examination of the spine gave normal results. To complete the study, attempts were made to obtain some spinal fluid, but several punctures between the third and fourth lumbar vertebrae were invariably dry. The Wassermann reaction of the blood was negative.

The diagnoses considered were the following: a tumor compressing the cord, myelitis, disseminated sclerosis, hemorrhage, syphilitic pachymeningitis and combined sclerosis. In view of the inability to obtain spinal fluid, which would have helped in the diagnosis, intraspinal injections of iodized poppy seed oil 40 per cent were proposed, but the patient refused consent. Therefore, the diagnosis was difficult. Rosett's test for induced tetanic myoclonia and Fay's test for sympathetic vasomotor phenomena gave negative results. In considering every possible diagnosis, the conclusion was reached that the compression of the cord was due probably to the presence of a tumor at the level of the third and fourth lumbar segments which correspond to the twelfth thoracic and first lumbar vertebrae. The presence of a Brown-Séquard syndrome, namely, sensory disturbances on the left and motor disturbances on the right, favored the localization of the tumor on the right side. Since at first an operation was rejected by the patient's family, intraspinal injections of magnesium sulphate were given for some relief from the persistent pain. The results were satisfactory. Nevertheless a radical operation was insisted on and was finally accepted.

Dr. Robert Boyer performed a laminectomy at the aforementioned level, and a tumor was found compressing the right side of the cord. Histologically, it was a benign fibroblastoma. The results of the operation were satisfactory. At first the pain was greatly relieved and at the time of writing, it had almost entirely disappeared. The disturbed sensation also improved, but the paralysis of the right leg remained unaltered.

The case is instructive from several standpoints: (1) in spite of seven years' duration of symptoms, some relief may be obtained from operative procedures; (2) a diagnosis and an accurate localization may be made from a purely clinical analysis of the few symptoms present; (3) it is well to bear in mind the absolute uselessness of the multiple operative procedures that are not infrequently carried out before a neurologic survey is undertaken. In the present case, the patient had undergone serious abdominal operations besides the removal of teeth and tonsils.

#### CYSTIC GLIOMA (SYRINGOMYELIA) INVOLVING THE POSTERIOR COLUMNS, WITH OPERATION. DR. M. J. COOPER.

In this case, the point of principal interest is the indication of extensive involvement of the posterior columns in a syringomyelic process, with comparatively slight involvement of the other tracts of the cord during the earlier period of observation.

A boy, aged 18, was first admitted to the service of Dr. Charles H. Frazier at the University Hospital for the study of a suspected thyroid dysfunction. These studies gave negative results, so far as disease of the thyroid was concerned, and the patient was transferred to the service of Dr. Spiller on June 13, 1930. From a neurologic standpoint, the interesting features of the history were the following: The patient had had sharp pains between the shoulder blades, radiating down the arms, since November, 1929 and occipital headache, a girdle sensation at the lower left costal margin and pain and a subjective sense of stiffness of the left knee since the early part of May, 1930. The interscapular pain later disappeared spontaneously. There had been vasomotor and secretory disturbances in the extremities for possibly a year or more.

Examination revealed that he could take only a few steps without aid, because of extreme ataxia. The Romberg test showed marked swaying, and the sensations of passive movement and position, vibration and of compass point discrimination were greatly impaired in both lower extremities. Sensations of touch, pain, heat and cold were slightly diminished in parts of both lower extremities, particularly on the right, and on the lower part of the trunk. There was a band corresponding to the ninth thoracic dermatome, on the left side, in which epicritic and protopathic sensations were greatly diminished; that level was the upper limit of the sensory changes. The deep reflexes of the lower limbs were exaggerated; there were abortive ankle clonus and patellar clonus on each side and a loss of the abdominal reflexes, but the voluntary motor power of the limbs was good, and there was considerable doubt that any loss of power had occurred. The Babinski sign was negative. The face, the upper part of the trunk and the upper extremities showed no motor or sensory changes.

The intraspinal pressure was found to be 13 mm. of mercury, and the Queckenstedt test indicated a block of the circulation of the cerebrospinal fluid. The fluid had a marked amber color and a high protein content, the protein being 52 units, as measured by a scale on which the normal content was 1.5 units.

For two weeks the sensory changes increased, but the motor power remained relatively unimpaired. Examination by Dr. Spiller on June 27, showed that the patient's incoordination had become so extreme that he could not take a single step, yet the voluntary motor power of the lower extremities was so well preserved that movements of the legs and thighs could not be prevented by the resistance of the examiner. The sense of vibration was lost as high as the patella on each side, and the patient had no recognition of passive movement of the toes or even of the ankles. The area of diminution of the sensation of pain had increased upward and at that time involved the first and second thoracic dermatomes on each side. The case was referred by Dr. Spiller to Dr. Frazier with a diagnosis of tumor, possibly arachnoiditis, which involved the posterior columns and to a much less extent the lateral columns.

On July 8, following an intraspinal injection of iodized rape seed oil and a roentgenologic examination, Dr. Frazier performed a laminectomy and decompression. The transverse processes of the fourth, fifth, sixth and seventh thoracic vertebrae were removed. On opening the membranes, it was found that the cord completely filled the dural sac and appeared cystic at the midpoint of the incision. A medial incision was made into the cord, and at about 0.3 cm. from the surface the cyst cavity was entered; yellowish fluid escaped. The cyst measured 5 cm. in length. A strip of gutta-percha tissue was inserted to prevent closure of the cavity. The operative diagnosis was cystic glioma of the cord. After microscopic study, Dr. Alpers reported that the tissue had some of the features of an astrocytomatous tumor or that it may have represented glial reaction about a tumor or cyst.

During the ensuing two months, there occurred a definite improvement in the sensations of position and vibration in the lower extremities, and the slight impairment of epicritic and protopathic sensations became less. A Babinski reflex appeared, and the motor power became somewhat less than it formerly had been. Two months after operation the patient was able to walk a short distance with little assistance. Following this, however, there was a recurrence of interscapular pain, and within a week the strength of the lower limbs, particularly in movements of flexion of the hips and knees, had become greatly impaired.

At the time of writing the patient showed a greater degree of diminution of epicritic and protopathic sensations in the trunk, from the second thoracic to the twelfth thoracic dermatomes, inclusive, and a considerable loss of deep sensibility in the lower extremities. There is great loss of power in the lower limbs.

In this case a differential diagnosis between cystic glioma and syringomyelia is difficult. One who has examined many microscopic sections of syringomyelia recognizes that often the cavity is surrounded by glial proliferation that may have distinctly the appearance of tumor. The length of the cavity varies in syringo-

myelia. In the case reported nothing is known of the boy's condition previous to the onset of pain between the shoulders. He may have had symptoms of involvement of the posterior columns long before the onset of the pain. It is impossible to judge from the observations at the operation the character and extent of the lesion. For these reasons it has seemed more prudent not to attempt to make a differential diagnosis between cystic glioma and syringomyelia.

## DISCUSSION

DR. C. H. FRAZIER: It has been only within comparatively recent times that syringomyelia has been regarded as a subject suitable for surgical intervention. In April, 1930, I had my first experience with this condition; the patient had had syringomyelia for fifteen years, and I regret that I had not accepted the suggestion of Spiller, who many years previously called my attention to the possibilities of surgical intervention in syringomyelia. In looking over the literature in July, 1930, I found only twelve surgical experiences recorded. The first recorded operation for syringomyelia was reported by Puusepp in 1926 (*Rev. neurol.*, 1926, no. 6) and since the appearance of his report there have been only four other articles on the subject. One by the same author (*Arch. franco-belges de chir.*, 1927, no. 4), one by Foerster (*Zentralbl. f. Chir.*, 1929, vol. 56), one by Schmieden (*Zentralbl. f. Chir.* 56:2114, 1929) and one by Oppel (*Arch. f. klin. Chir.* 155:416, 1929). Briefly, the results were as follows: Puusepp operated in four cases with manifest improvement. Oppel recorded seven operations with results varying from negative to brilliant.

In my case, the patient was seriously handicapped; the disease was of long standing, and one upper and one lower extremity were spastic and paretic; he was fast losing the power of the other arm. Only recently he had become incontinent, and it was chiefly in the hope of restoring vesical control and possibly relieving the spasticity of the arm and hand that, after consultation with Dr. Spiller and the attending neurologist, Dr. Timme, the operation was undertaken. The incontinence was relieved immediately, and a considerable range of usefulness was restored to the arm. Furthermore, the patient could hold the head erect, which he could not do before, and enjoyed a sense of relaxation which had replaced that of tension.

From my experience and that of others, there should be no question as to the propriety of surgical intervention in syringomyelia, even though in some cases the results are more striking than in others. If operation is to be done, it should not be delayed too long.

There is little that offers itself for discussion concerning the technic. I question an attempt to give arbitrary directions as to the point of drainage. Two sites have been proposed; one, 2 mm. to the right or left of the midline, the other on the lateral aspect of the cord. I believe that the operator should be influenced by the point at which the cyst appears to come nearer the surface and this point will vary in different cases.

A second question in technic has to do with permanency of drainage; the insertion of a thin strip of gutta-percha in the artificial stoma to insure permanent drainage. I believe that this is a wise precaution, and a foreign material such as gutta-percha should serve the purpose better than a piece of the patient's tissue such as the strip of dura which Oppel employed.

A third question is: Should the dura be sutured? I am inclined to believe that in the future I would not suture the dura, especially if, before the operation, there was a definite spinal block.

In the case presented by Dr. Cooper, I was disposed to believe at the time of operation that I was dealing with a cystic glioma, and I am quite sure that in this case the patient would have enjoyed a longer period of relief had the dura been left unsutured.

DR. W. G. SPILLER: The interesting feature in this case was the intense incoordination in the lower limbs. This was so great that the boy was unable to stand without support, even with the feet far apart, and although he could

move his legs he would pitch forward to one or the other side in attempting to walk. The lower limbs could be moved freely while he was in bed, and it was difficult to prevent voluntary movement of these limbs by the hand of the examiner. A diagnosis of tumor or arachnoiditis of the posterior columns, with little involvement of the lateral columns, was made, and this diagnosis was confirmed by the operation.

Cases of endogenous lesion confined or nearly confined to the posterior columns in my experience are rather rare. I had another case about a year ago. A woman, aged 61, in the latter part of 1928 experienced tingling in the fingers; she was unable to pick up small objects. The power of voluntary movement in either lower limb against resistance of the examiner was normal. Position and passive movement sensations in each big toe were greatly affected. Vibratory sensation was greatly impaired below the thoracic region. She swayed considerably in standing with the feet together when the eyes were open but more so when the eyes were closed. The patellar and achilles reflex on each side were feeble. This I attributed to implication of the reflex collateral fibers in the posterior columns when no degeneration of the crossed pyramidal tracts was present to remove inhibition and permit reflex action. Examination of the blood showed: red cells, 3,600,000; white cells, 5,100; hemoglobin 80 per cent; moderate anisocytosis, moderate poikilocytosis and moderate polychromatophilia. Analysis of the contents of the stomach gave no free hydrochloric acid and little total acidity.

I made a diagnosis of posterolateral sclerosis of the anemic type, but with the lesions confined to the posterior columns. This diagnosis was correct. The typical lesions of this condition were found in the more central part of each posterior half of the posterior columns and did not extend to the posterior horns or posterior border of the spinal cord in the lumbar and thoracic regions, but were more extensive in the cervical region. The lateral columns were intact even with the Marchi stain. I have since found one or two similar cases with necropsy in the literature. I have also had cases of posterolateral sclerosis of the anemic type in which the symptoms indicated involvement of only the lateral columns.

DR. M. Q. COOPER: Dr. Holmes has asked what the roentgen examination showed after the injection of iodized rape seed oil, and what condition was found in the upper part of the cord at operation. Dr. Frazier's report of the operation stated that the marking that was made on the skin was identified as being opposite the spinous process of the sixth dorsal spine. After the injection of iodized rape seed oil, the roentgenogram showed that it had divided into two columns at the level of the eighth dorsal vertebra, and two columns, one on each side, ascended for a distance of from two to two and a half vertebrae. The operative incision extended from the fourth to the seventh vertebrae, inclusive, and the cyst was at the middle of the incision. I do not know what exploration was made above the level of the fourth thoracic vertebra at the time of operation or whether there was evidence of a cavity containing fluid above that level.

#### THE LAURENCE-BIEDL SYNDROME: REPORT OF A CASE. DR. STUART N. ROWE.

P. F., a white woman, aged 37, entered the Philadelphia General Hospital, on the service of Dr. Charles W. Burr, because of a paralytic stroke that had occurred about one week prior to admission. However, in the course of examination it became apparent that she was also suffering from a somewhat unusual combination of endocrine disorders, and it is chiefly from this point of view that she is here presented.

It had been possible to investigate only three generations of the Russian Jewish family of the patient. Her father and maternal grandfather died of apoplectic strokes. In the two older generations there was no history of polydactylism, blindness, adiposity or feeble-mindedness, although the patient's mother was apparently of only moderate intellectual ability. There were three children in the family. Pearl, the eldest, was the patient. Harry, aged 32, had been blind since the

age of 12 months; he was abnormally obese, and had one extra little finger on each hand and an extra toe on each foot. He was a graduate of the Overbrook School for the Blind and was able to support himself by running a news stand. Sophie, the youngest child, was a graduate of high school and a business institute and was apparently entirely normal.

According to the mother's statement, Pearl was a full term baby, delivered normally. She had her first tooth at 6 months, talked at 2 years, and walked at the age of 3. At 5 she was sick for some time with diphtheria. The following year she went to school but did not seem to get on well, and a medical examination revealed a hitherto unsuspected blindness, for which she was sent home. The mother is positive that the child could see for a few years and then gradually lost her vision, until the complete blindness which was now present set in. The patient has remained at home since, helping a little with the housework. So far as the mother knows, the girl's menstrual periods, which began at the age of 13, have been regular and of average duration and amount. She has always been abnormally fat.

On examination, the patient appeared obese, with a staring, expressionless, childish face and an abnormal growth of hair on the chin. The voice was high-pitched and monotonous. She was 5 feet 2 inches (157.48 cm.) in height and weighed 134 pounds (60.8 Kg.). On admission, the blood pressure was 220 systolic and 120 diastolic. The thyroid gland was not enlarged or nodular. The heart and lungs were normal. The excessive adipose tissue was distributed chiefly about the breasts, girdle and mons pubis, the extremities being relatively short but not markedly fat. The patient's hands showed not only a myxedematoid puffiness and short tapering fingers, but also a peculiar flushing of the palmar surfaces.

A gynecologic examination revealed a thick hymen with only a small perforation, thus preventing bimanual palpation. The external genitalia were otherwise essentially normal.

The report of an ophthalmologic study was as follows: ptosis of the left upper lid; vertical nystagmus of both eyes; unequal pupils (right 4 mm. and left 3 mm.) which reacted slightly to light and convergence. Tension was normal. Opacities, pinhead in size, were found centrally in the lens of each eye. Both optic nerves were atrophic, and there was retinitis pigmentosa in both eyes, more pronounced on the left.

The hospital psychologist reported that the patient's mental age was about 5 years.

From a neurologic point of view, the chief feature was a flaccid type of hemiplegia on the right side, including a lower facial weakness. The extremities showed little change during the patient's stay in the hospital, but speech improved considerably.

In the course of laboratory studies done as a routine measure, it was discovered that the blood sugar was high, and the patient is under dietetic and insulin treatment. The remainder of the laboratory results were essentially negative. Roentgenograms of the skull showed no change in the size or shape of the sella turcica, but there was some rarefaction of the posterior clinoid processes. Roentgen studies of the hands and feet showed no abnormalities. The patient refused to cooperate in an attempt to determine the basal metabolic rate.

The final diagnoses in this case were: (1) cerebral thrombosis with hemiplegia on the right side, (2) hypertension, (3) hyperglycemia and (4) dystrophia adiposogenitalis with retinitis pigmentosa or the Laurence-Biedl syndrome.

#### DISCUSSION

DR. A. M. ORNSTEIN: The presentation of Dr. Rowe's case has timely interest for me because I have in preparation a report of three cases of the Laurence-Biedl syndrome. Besides the patients of Solis-Cohen and Weiss, another contribution from Philadelphia was made in 1923 by Dr. de Schweinitz, who may tell us something about the *raison d'être* for the almost constant association of

retinitis pigmentosa and the Froelich symptom-complex. This phase of the subject interests me especially because I have explained in my own mind this association on an embryologic basis. The optic chiasm and the infundibulum take origin from the ventral segment of the ectopic zone surrounding the primary optic vesicle. It is stated that within the optic chiasm are efferent fibers of the retina that regulate the chemical function of the pigment cells. If a defect in the evolution of this segment of the primary neural type occurs, both the optic chiasm and the hypothalamus may be the seat of abiotrophic changes resulting in adiposogenital dystrophy, optic atrophy and pigmentary degeneration of the retina. It would seem possible on this basis that the conception of a genotypic unit character may be the explanation of the two chief phenomena of the Laurence-Biedl syndrome.

DR. G. E. DE SCHWEINITZ: E. Treacher Collins has suggested that the primary change is abiotrophy, that is, a degeneration of the tissues, due to defective vitality of the retinal neuro-epithelium. Pigmentary degeneration of the retina in association with polydactylism has long been known and was described fifty or more years ago. This association with a disorder of the pituitary body has come into prominence in comparatively recent times, and the syndrome described so accurately by the essayist is well known.

It should be remembered, however, that there may be an association of pigmentary degeneration of the retina, polydactylism and pituitary body dysfunction, without mental disturbance or inferiority. A patient under my care from early childhood with these conditions, in spite of visual and other handicaps has done remarkably well at school in preparation for college.

DR. E. WEISS: The condition compares closely with the cases reported by Dr. S. Solis-Cohen and myself in 1925, to which we gave the name Laurence-Biedl Syndrome, in honor of the English ophthalmologist Laurence who, so far as we could determine, was the first to call attention to the condition, and Biedl, who added to the description of the syndrome and suggested its origin in certain cerebral centers. Though we recognized the general inadvisability of using proper names to designate this syndrome, it seemed justified rather than to use such a cumbersome name as "dystrophia adiposogenitalis with atypical retinitis pigmentosa, polydactylism, and mental deficiency." Since our report a number of additional cases have been recorded. One feature to be emphasized is that the syndrome occurs in familial groups. Our patients were four of a family of eight children, and a number of similar reports are available.

It would seem that the retinitis pigmentosa is merely one of a number of anomalies originating from the same cerebral source. Most authors are agreed that this source is located in the basal centers of the midbrain, rather than in the pituitary gland as heretofore believed. From the number of typical cases recently reported and others which present but two or three of the anomalies grouped in the syndrome, it would seem that the condition is much more common than the forty-five or fifty cases so far recorded in the literature would lead one to believe.

DR. S. N. ROWE: In some cases, pituitary therapy has been used with definite improvement. In one case a definite gain in mental ability of the patient was obtained, and I hope to try out something of this type with this patient.

#### INCOMPLETE EXTERNAL OPHTHALMOPLÉGIA. DR. J. M. COOK.

The patient entered the service of Dr. Spiller in the University Hospital on Sept. 10, 1930, complaining of ptosis of the right eyelid, inability to move the right eye and generalized weakness. Three years ago, he had a cold, with a sore throat and backache. During the next three months, paralysis of the external rectus muscle of the right eye and progressive diplopia gradually developed. During the following year and a half, in the course of which he did no work, these symptoms gradually disappeared. He returned to work about Christmas, 1929. Shortly thereafter he had a chilly sensation up and down the back, and the former symptoms of the eye reappeared, along with ptosis of the right eyelid.

This progressed during the next two months to complete ptosis of the right eyelid, total inability to move the right eye outward and marked limitation of motion in other directions. Simultaneously a condition of rapid fatigue on exertion developed; this would disappear after a night's rest, but effort would soon exhaust him. He was somewhat weaker on the left side, falling twice because the left hip gave way. He could not hold his arms above his head, and they would drop slowly from the height to which he could raise them. He was forced to quit work again ten weeks before admission. After this he regained some ability to move the right eyeball inward, upward and downward, and also some strength.

The only significant point in the past history is that he was subject to colds. He had worked as a cleaner of soup kettles for fifteen years and was often soaked about the neck and shoulders.

On admission, the positive physical signs were the following: a general weakness on voluntary movement of the extremities, more marked in the left upper extremity and a slight impairment of diadokokinesis in both hands, a little more marked on the right. The eyes were prominent. There was total paralysis of the external rectus muscle of the right eye, marked paralysis of the superior rectus muscle and slight paralysis of the internal and inferior rectus muscles. There was partial but marked ptosis of the right upper lid, marked weakness of the orbicularis oculi muscle on the right and diplopia on distant point fixation, except when looking at a point in front and slightly to the left. The fields and fundi were normal. Vision was 6/9 in both eyes. The triceps reflex was absent on both sides; the abdominal reflexes were slightly reduced on the left, the patellar reflexes were markedly hyperactive and about equal, and the achilles reflex on the left was slightly hyperactive.

During his stay in the hospital, he had been given inunctions of mercury for a period of three weeks (until dermatitis forced a cessation) and potassium iodide, without improvement. Weakness of the external rectus muscle of the left eye developed so that he could not rotate the eye outward to the full extent, and when he did rotate it outward, a lateral nystagmus appeared. Following the onset of a cold, the ptosis of the right eyelid became slightly worse. Vision had become reduced in the right eye from 6/9 to 6/12. General muscular power had improved to some extent. The genito-urinary department reported a marked excess of pus in the prostatic secretion, which became normal after three prostatic massages. The nasopharyngeal report showed the septum moderately deviated to the right, but not obstructed, and a hypertrophic mucous membrane over both middle and lower turbinates. The patient had badly infected tonsils and a chronic pharyngitis. The urine was normal except for a slight increase of leukocytes. The blood count was normal. The roentgenologic report showed a slight atrophy of the dorsum sellae but no other signs of tumor. The Wassermann and Kahn tests of the blood gave negative results.

Lumbar puncture showed a clear fluid with an initial pressure of 185 mm. of water. On coughing and straining there was a rise to 270 mm., falling rapidly to the initial pressure. On unilateral jugular compression, there was a rise to 209 mm. and on bilateral jugular compression to 450 mm., in each case falling promptly on release of pressure. The spinal fluid contained 1 cell and 0.2 units of protein. The Wassermann and colloidal gold tests gave normal results. It has been suggested that these observations may be due to: (1) tumor, (2) syphilitic meningitis, (3) encephalitis.

#### DISCUSSION

DR. W. G. SPILLER: The paralysis includes all the external ocular muscles of the right eye and possibly in mild degree the external rectus muscle of the left eye. There is no paralysis of associated ocular movement, and this indicates that the posterior longitudinal bundles probably are intact. Collier recently has referred to the frequency of paralysis of the ocular muscles from a lesion at the sphenoidal fissure and has attributed this "sphenoidal fissure syndrome" occasionally to cold alone but more frequently to the spread of inflammation from septic sinusitis. He refers to frequent paralysis of the oculomotor nerves in diabetes.

The patient presented did not have glycosuria. He had been much exposed to water, as he has stood in water, and he stated that his ocular symptoms began with a cold. He had chronic rhinopharyngitis, but no evidence of sinus disease. Although he had no involvement of the ophthalmic division of the fifth nerve, I have thought of the possibility of the "sphenoidal fissure syndrome" in this case with escape of the ophthalmic branch of the trigeminal nerve.

It is difficult to attribute the almost complete unilateral external ophthalmoplegia to disease of the nuclei, as no other cranial nerve nuclei are involved. In a paper published, in 1919, in the *American Journal of the Medical Sciences*, I expressed the view that a lesion that destroyed the nuclei of the third and fourth nerves bilaterally, breaking the supranuclear connections, and involving the posterior longitudinal bundles, might also cause paralysis of the sixth nerves through the connection of the posterior longitudinal bundles, without any lesion of the sixth nerves or their nuclei. In 1924, I published in *Brain* the report of another case which bears out this supposition. It was a case of ophthalmoplegia internuclearis anterior, with necropsy, and seems to be the only case with necropsy in the literature. Softening in each posterior longitudinal bundle at the level of the fourth nuclei was the lesion found. The patient had been unable to contract either internal rectus muscle in associated lateral movement but could do so in convergence. The external rectus muscles were not affected. It would seem at first thought that this case is a contradiction to my view published in 1919, but in the case reported in 1924 there was not complete destruction of the posterior longitudinal bundles, convergence movement was preserved, the oculomotor nucleus on each side was intact, and only the inner portion of each posterior longitudinal bundle was degenerated. Collier has expressed similar views in *Brain* in 1927.

#### MOVEMENTS OF THE EYEBALLS. DR. GORDON HOLMES.

This paper will be published in full elsewhere.

#### THE ARGYLL ROBERTSON PHENOMENON. DR. W. G. SPILLER.

Dr. Spiller referred to his paper on "Argyll Robertson Phenomenon" read at the previous meeting of the Philadelphia Neurological Society in May, 1930, and which appeared in the *ARCHIVES OF NEUROLOGY AND PSYCHIATRY* (24:566 [Sept.] 1930). He said that in his textbook on the diseases of the eye, de Schweinitz evidently accepts the statement that with the pupilloscope an early stage of the Argyll Robertson phenomenon may be detected when it cannot be recognized without this or a similar instrument. It is interesting to have Dr. de Schweinitz express his views on this subject, as the belief is widespread that in the Argyll Robertson phenomenon the inaction to light must be complete.

#### DISCUSSION

DR. G. E. DE SCHWEINITZ: As Dr. Spiller has pointed out, it is not uncommonly believed that complete abolition of the light reflex of a miotic pupil must exist in order to justify the diagnosis of the Argyll Robertson phenomenon. At least this is the inference drawn from various published reports. He maintains that this is an error, in that "all preliminary stages to the production of an Argyll Robertson pupil are ignored." His contention in this respect is correct.

Much depends on the method of examination and the character of light employed, and these factors should be stated in the records of any investigation of the pupil reflexes, as Dr. Spiller further properly insists. Fairly satisfactory results can be obtained if the source of illumination is a narrow beam of electric light, secured by means of a Wurdemann transilluminator on which a cap containing a small condensing lens is fitted, as in the model designed by Veasey. Hans Barkan, however, maintains that with Carl von Hess' differential pupilloscope (*Arch. Ophth.* 51:29 [Jan.] 1922), anomalies of pupil reaction can be detected that are not discoverable by other methods. I am not practically familiar

with this instrument, but, as pointed out by Bedell and Feingold, accurate observations can be made with the aid of a slit-lamp, the light being turned off and on while the iris and pupil area are studied with the corneal microscope. The faintest reactions can be detected. I have often employed this method with entire satisfaction and have been able to note slight reactions that had not been detected when the ordinary technic of investigation of the pupil was used.

TRAUMATIC PNEUMOCEPHALUS. DRS. S. W. MILLER, R. N. KLEMMER and P. O. SNOKE.

The tremendous increase in cranial injuries since the advent of the more rapid means of transportation, such as the automobile and airplane, has served to demonstrate the inadequacy of our knowledge of the nature, extent and treatment of certain of these injuries. We are reporting the following case because of the great damage sustained by the cerebrum with at least temporary infection, the associated spontaneous introduction of air into the ventricles, operation and complete recovery.

W. F., aged 20, a white man, was admitted to the Lancaster General Hospital on Sept. 29, 1928, following an automobile accident. There was profuse nasal

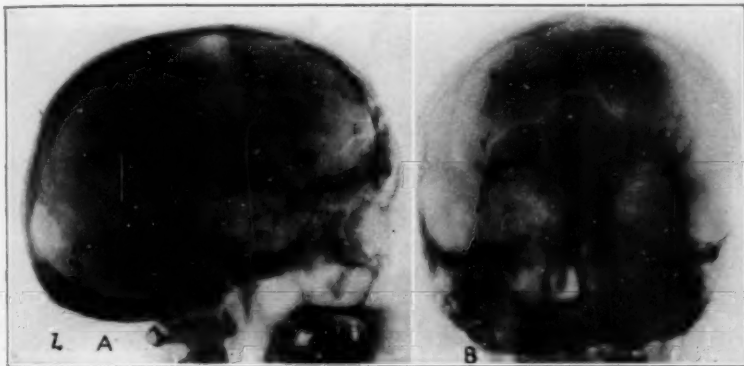


Fig. 1.—Roentgenograms taken Sept. 29, 1928. Note the involvement of both frontal sinuses in lines of fracture. There is no intracranial air. A, indicates the left side of the head; B, the right.

bleeding; both eyes were ecchymotic and numerous lacerations covered the face and hands. He was unconscious and restless. Roentgenograms showed multiple fractures of the frontal bones with lines of fracture extending into both frontal sinuses and both orbital plates (fig. 1).

One week elapsed before he regained consciousness. A lumbar puncture at this time showed nothing abnormal except a few red blood cells. On the thirty-second day of convalescence, he complained of severe headache and a watery rhinorrhea that occurred transiently when he sat up. He was afebrile and was discharged as cured on Nov. 5, 1928, the rhinorrhea having ceased.

Fourteen days after discharge, fifty-one days after the accident, he was readmitted, complaining of severe headache, fever and recurrence of the watery rhinorrhea in increasing amounts. Clinically, there was photophobia, a rigid neck and ptosis of the left eyelid. The Kernig and Babinski signs were negative. Sneezing was an occasional symptom. The patient said that he blew his nose vigorously. Rhinorrhea was noticeable while he was lying on either side, but was more decided on raising the head. The discharge was from the left nostril only. On turning the head the patient described a sensation similar to "water gurgling in a bottle." At no time during the course of the disease were there

any convulsions. The temperature rose from 100.2 F. in the morning to 103 F. in the afternoon. A blood count revealed 17,100 white blood cells. Two lumbar punctures were performed on the day of readmission, less than twelve hours apart. The first showed 8,200 cells, the second 20,700 per cubic millimeter. A differential smear showed the cells to be entirely of the polymorphonuclear variety. A fourteen hour culture of the cerebrospinal fluid showed a growth of streptococci. On each of the three following days, 20 cc. of antistreptococcic serum was given intravenously. The fever subsided, and the cerebrospinal fluid cell count fell to 650.

Twenty days after the accident, roentgenograms were made with the patient in the Law frontal sinus position. At least 50 cc. of cerebrospinal fluid poured from the left nostril during this procedure. The patient was rational and cooperative, but complained of severe headache. Films showed subdural air in the right frontal region and complete delineation of the left lateral ventricle and the third ventricle (fig. 2).

In view of the fact that we considered operation imperative and since the meningitis was improving, he was transferred to Dr. Dandy's service at the Johns Hopkins Hospital.

At the operation, on November 24, using a transfrontal approach and elevating the fragments, Dr. Dandy reported that air was seen to bubble through the roof

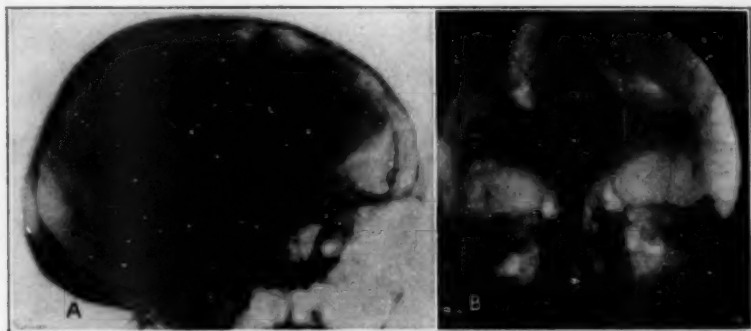


Fig. 2.—In *B* (right side) note the dilatation of the ventricle in the antero-posterior view and subdural air in the right, in *A* (left side) note the change in the size of the anterior horn with the change in the position of the head.

of the orbit, and a large bony fragment, a portion of the roof of the left orbit, was lifted out. About 3 cm. posterior to the supraorbital ridge, there was a rent of 2 cm. by 1 cm. in the dura. Beneath the dura, in the subarachnoid space a well walled-off channel extending upward into the brain substance and communicating with the left lateral ventricle at this point had developed.

A piece of fascia from the thigh, 5 by 5 cm., was sutured into the dural defect. The loose fragment of bone was replaced and the incision closed. The patient made a complete recovery.

On examination on May 7, 1930, the patient reported that he had been continuing his occupation as silk weaver and was free from symptoms except for loss of the sense of smell. The sensation of smell had been present up until the time of operation. There were no physical abnormalities except a slight left enophthalmos.

*Resumé of Literature:* In 1926, Dandy (Pneumocephalus, *Arch. Surg.* 12:949 [May] 1926) reported three cases of intracranial pneumatocele, and in reviewing the literature found twenty-five other cases. Of these twenty-eight cases, eight definitely showed air in the ventricles. In several others there was considerable doubt as to the location of the air. Our patient is apparently the eleventh reported

in which air was proved to be in the ventricles and the seventh patient who has survived. The following table shows recoveries after intraventricular pneumatocele.

*Mechanics of the Introduction of Intraventricular Air.*—Wodarez (Zur Kasuistik der intercranieller Pneumatozele, München. med. Wchnschr. 62:968, 1915) and Duken (Two Cases of Intracranial Pneumatocele Following Bullet Wounds, München. med. Wchnschr. 62:598, 1915) presupposed a valvelike action permitting egress of fluid and ingress of air. In our case there was a dural defect so large that a valvelike action was improbable, and it was not found at the operation.

Dandy (*Arch. Surg.* 12:949 [May] 1926) believed that an additional factor such as sneezing, coughing, straining or even swallowing is necessary to force the air from a sinus through rents in the bone and dura into the brain proper. In our case, sneezing was a fairly prominent symptom and probably materially aided the formation of the channel from the rent in the dura through the brain substance to the lateral ventricle. It would seem that the cerebrospinal fluid drained through the fistula in much the same manner that water drains from a narrow-mouthed bottle when it is inverted.

Sneezing followed by rhinorrhea is almost pathognomonic of pneumocephalus. These symptoms, however, may be absent in the condition. They may be combined with any of the more commonly accepted indications of cerebral injury such as headache, stupor, etc.

Table Showing Recoveries After Intraventricular Pneumatocele

Case Reported by	Cause of Condition	Cranial Air Sinus Involved	Recovery
1. Wolff, 1914.....	Bullet	Frontal	Operation
2. Potter, 1919.....	Fracture	Frontal	Spontaneous
3. Teachnor, 1923.....	Fracture	Mastoid	Spontaneous
4. Dandy, 1925.....	Fracture	Frontal	Operation
5. Dandy, 1925.....	Fracture	Mastoid	Spontaneous
6. Davidson, 1927.....	Fracture	Frontal	Spontaneous
7. Miller, 1928.....	Fracture	Frontal	Operation

The important instructive features of the case are four: (a) increasing headache in a patient with fracture of the skull should call for roentgenographic reexamination; (b) in fracture of the skull involving a sinus, patients should be instructed never to blow the nose; (c) operative interference in cerebrospinal fistula is usually necessary; (d) the roentgenogram is diagnostic.

## NEW YORK NEUROLOGICAL SOCIETY AND NEW YORK ACADEMY OF MEDICINE, SECTION OF NEUROLOGY AND PSYCHIATRY

Joint Meeting, Nov. 17, 1930

LOUIS CASAMAJOR, M.D., *President, New York Neurological Society, in the Chair*

CLINICAL PRESENTATIONS FROM THE NEUROLOGIC SERVICE  
OF THE MOUNT SINAI HOSPITAL. DR. ISRAEL STRAUSS.

TRANSITIONAL CELL CARCINOMA OF THE POSTERIOR PHARYNX (SCHMINKE  
TUMOR).

A. F., a woman, aged 31, began to complain of pain in the left ear two years before presentation. She was examined by a local physician who told her that there was nothing wrong with the nose and that she had "neuralgia." The antrum was irrigated at the Israel Zion Outpatient department. Following this, a

purulent postnasal discharge developed. The pain became worse, and deafness began to develop in the left ear. This was in December, 1928. She then went to the Neurological Institute where a diagnosis of pansinusitis was made.

On July 1, 1929, she came to the Mount Sinai Hospital because of the intractable pain which at that time was felt in the left ear, the temporal and occipital regions, the left side of the face and in the hard palate on the left. The pain was described as "nagging." Examination at that time showed hypalgesia of the left half of the lower lip, inability to open the mouth widely, slight left facial asymmetry, and retraction of the ear drum on the left side with bone conduction deafness on this side—evidences of disease of the ear secondary to the nasal operations. Roentgenograms showed cloudiness of the antrums and sphenoids. There was a postnasal drip. A sphenoid-ethmoidectomy was advised, which the patient refused. She was discharged on July 30, with a diagnosis of sphenopalatine neuralgia on the basis of a sinusitis.

After this, injections were made into the maxillary nerve without relief. The pain and purulent discharge became severe in the following October. Examination at that time revealed a mass near the sphenoid and mastoid, and a biopsy showed carcinoma of the nasopharynx. A roentgenogram showed rarefaction of the ethmoidal region. The patient was then given four implantations of radium in December. The pain and discharge were momentarily relieved, but returned, and a radical ethmoidectomy was advised, but not performed.

On April 28, 1930, the patient was readmitted to the Mount Sinai Hospital complaining of continuous pain in the left temporal and supra-orbital region, pain in the left eye and diplopia on looking to the left. The diplopia had appeared about a month before hospitalization. Examination showed: normal fundi; weakness of the left external rectus, causing diplopia; weakness of the left motor trigeminal nerve with involvement of sensation in the second and third branches; a purulent discharge from the left nostril, with postnasal drip and a thickening of the drum on the left; normal caloric tests, and bone conduction deafness on the left, with tinnitus. There was loss of taste over the anterior two thirds of the tongue on the left. There were minute hard nodules high up in the left side of the nasopharynx. The larynx was normal.

Examination of the skull and sinuses showed marked density throughout the left ethmoidal region, extending into the sphenoid. The density was much greater than that seen from ordinary infection.

Subsequently there was definite increase in the weakness of the motor trigeminal nerve with more marked deviation of the jaw to the left. The left side of the soft palate moved slightly, and the uvula was drawn over to the right. There was hypesthesia over the lower two thirds of the left side of the face with analgesia and thermohypesthesia. Paralysis of the left external rectus muscle developed. In May, another biopsy showed transitional cell carcinoma.

On May 24, radium seeds were implanted in the region of the sphenoid-ethmoid. The following morning, the patient complained that she could not see with the left eye. Examination revealed the loss of macular vision on the left with preservation of peripheral vision and no changes in the macula, indicating some pressure on the optic nerve. The pupils were equal, the left pupil was fixed to light, the right reacting sluggishly; both, however, reacted promptly in accommodation. The left eyelid was held in a position of ptosis, but there was no real weakness. The patient vomited frequently.

On May 29, the seeds were removed. On June 3, examination revealed complete amaurosis in the left eye, with vision in the right of 10/10 and normal fundi. The patient was discharged on June 4 to return in four weeks for further roentgen treatment. It was thought that the loss of vision in the left eye would be permanent, and that it might be advisable to enucleate the eye and thus be in a position to apply radium more directly to the tumor.

In July, the patient complained of pain and burning sensations in the left cheekbone and side of the face. At times she heard what she described as a barking in the left ear. There was a bloody, purulent discharge from the left

nostril. Examination showed sensory diminution in the lower two thirds of the left side of the face and bilateral corneal analgesia. She had limitation in attempting to open the mouth, but no deviation of the jaw to either side. There was ptosis of the left eyelid and slight weakness in the left external rectus; total amaurosis in the left eye persisted.

On August 28, the patient complained of drowsiness, but not of headache or vomiting.

She was seen again in September, and showed fibrillations of the tongue and almost total immobility of the left side of the palate. She had lost 3 pounds (1.4 kg.) in a month and complained of suboccipital headache.

*Comment.*—In 1922, New, of the Mayo Clinic, reported seventy-nine cases of the type presented here. In these cases, seventy-four operations were performed before a correct diagnosis was made. The tonsils and adenoids were removed in twenty-four; glands of the neck in eighteen; wisdom teeth in twelve; intranasal operations were performed in nineteen, and a mastoid operation in one. Twenty-five of the cases eventually showed neurologic involvement. This report showed how difficult it is to make a correct diagnosis early in the disease and how frequently the neoplasm is overlooked. This is because the tumors may be very small in the beginning and are usually situated in the fossa of Rosenmüller and involve one eustachian tube. The history in our case is not at all unusual. It was the eventual appearance of a mass in the nasal pharynx that led to the correct diagnosis. The cranial nerve most frequently involved is the abducens. Objective disturbances in the distribution of the fifth nerve are common. The dissociations in sensation in this distribution are peculiar. It is generally the peripheral portion of the fifth nerve that is involved in the growth of the tumor, but occasionally the gasserian ganglion has been affected. It is not at all unusual to have the facial and acoustic nerves likewise attacked, and the ninth to eleventh nerves may be paralyzed by glandular involvement or by the proximity of the growth to the jugular foramen. As a rule, several nerves are affected simultaneously, especially in the sphenoidal fissure. These tumors grow usually along the base of the skull. Surgical intervention is of doubtful value because of the location and the extension in these cases. They are radiosensitive, and if they could be reached successfully by radium or deep roentgen rays, a cure could be accomplished. Gardham proposed an osteoplastic resection of the upper jaw in order that tubes of radium emanation might be inserted into the tumor along the base of the skull. Most of the patients died as a result of the extension of the growth and of metastases. While this patient has been improved by the treatment thus far given, I am not hopeful that the growth can be eradicated. We may consider the removal of the left eye so that through the orbit we may have better access to the tumor for the implantation of radium.

#### ACUTE SYPHILITIC MENINGITIS WITH RECOVERY.

W. N., a man, aged 44, was admitted to the Mount Sinai Hospital on June 27, 1930, complaining of headache, which was progressive, and visual disturbances. The face had a cyanosed flush. He said that he had not had syphilis. He had had a bubo nineteen years before presentation. Nine months before presentation, the Wassermann reaction was 4 plus. At that time he was struck on the head and was unconscious for six hours, with a resultant diplopia which lasted six months.

The patient became acutely ill two months before entering the hospital, when he began to have severe constricting headache of hatband distribution, more severe in the frontal and temporal regions bilaterally. This was severe and constant, but the severity was paroxysmal. It was accompanied by visual disturbances in the form of diminution of visual acuity and in recent weeks by light diplopia and sparkles of blue lights. The visual disturbance had made him markedly dizzy. The vertigo was relieved by closing the eyes and reclining. For many years, the patient had had increasing difficulty in hearing in the right ear, markedly so in the few weeks prior to presentation. There had been no tinnitus

or hyperacusia or discharge. There had also been some difficulty in swallowing. There had been no vomiting, no convulsions and no coma. The patient did not have chills or chilly sensations, aphasia, difficulty in phonation, paresthesia, numbness or cyanosis affecting any of the extremities.

On admission, the physical examination showed bilateral papilledema, general hyperreflexia, a slight weakness of the left upper extremity, pupils reacting sluggishly to light, the right pupil larger than the left, partial ptosis of the right eyelid, and nerve deafness on the right side with slight rigidity of the neck and a slight Kernig sign. The papilledema was from 3 to 4 diopters in height; the arteries were narrowed, and the veins were dilated and cyanotic. The spinal fluid pressure was 320 mm. (actual height in manometer); there were 110 cells, all lymphocytes, in the field.

The history of a positive Wassermann reaction in the blood, the papilledema, the increased spinal fluid pressure and the pleocytosis were regarded at once as indicating vigorous antisyphilitic treatment, in spite of the fact that the possibility of a neoplasm could not be excluded on the basis of the physical signs. The patient was given daily injections of corrosive mercuric chloride, careful attention being paid to the urinary output. This was followed by the administration of bismuth and neoarsphenamine. There was rapid response to the treatment with corrosive mercuric chloride. The patient's headache and meningeal symptoms disappeared.

He was discharged on July 26 and referred to the outpatient department for further treatment. At this time, the optic nerves still had an elevation of 3 diopters, but in places the edema had lessened and the exudates had disappeared. When he was examined on August 28, the swelling in the disk had entirely disappeared; the outlines were still somewhat blurred; the pupils reacted normally, and there were no objective signs of any involvement of the nervous system.

As you see him tonight, he appears and claims to be in perfect health. The fundi now show a slight blurring of the disks but no other pathologic change. He has been receiving antisyphilitic treatment regularly since discharge from the hospital. A case such as this, of meningeal and vascular syphilis, is not met with today as frequently as formerly. In our experience it requires active treatment, and in the beginning no agent is probably more efficacious than corrosive mercuric chloride when it can be given, as was done in this case, in daily doses under careful supervision. There is another advantage in this form of therapy in that it prepares the patient for the administration of the arsenicals. There is still in the minds of some a question as to whether or not patients with a choked disk should be given this active treatment on a syphilitic basis. We have never hesitated in regard to this, because we believe that despite the fact that optic atrophy has occasionally followed the administration of mercury or even of the arsenicals in cases showing an active inflammation of the nerve, this has been due to the disease and not to the treatment.

#### SUPRASellar NEOPLASM: DEEP ROENTGEN THERAPY WITH IMPROVEMENT.

S. S., a man, aged 30, was admitted to the Mount Sinai Hospital on July 19, 1930. The past history was without significance, except for a nasal operation ten years before. There was no history of obesity. One year prior to admission, he began to have increased thirst, causing him to drink much fluid and to urinate excessively, especially at night, so that he could not sleep. After two months, the sella turcica as shown in a roentgenogram, was thought to be slightly enlarged. He then used a nasal spray of solution of pituitary three times daily. After this, instead of voiding every hour a total of  $6\frac{1}{2}$  quarts daily, he voided every five or six hours and only rarely at night. About six months later, he noticed that his vision was getting poor. There were no palsies or particular areas of blindness. Since then he has had periods when the blurring of vision disappeared entirely for several weeks, only to return for a similar period. This persisted for a month before admission. He had diplopia for a short period about three months before entering the hospital. He has not had headaches, convulsions,

paralyses, auditory disturbances, anosmia, edema, excessive perspiration, fever or chills, gain in weight or mental changes. For ten months, he has been impotent. He has always felt slightly weak and is easily fatigued.

Physical examination revealed a rather slender man 5 feet 9 inches (175.3 cm.) in height with large hands and feet. The skin was thick, dry and of a peculiar pallor, and there was definitely increased bulk in the subcutaneous tissues. The hair was fine and rather sparse. There was very little pubic and axillary hair, and no hair on the body. The pubic hair was of a female distribution. The heart and lungs were normal. There was a dorsal kyphosis with compensatory scoliosis in the dorsal spine above and below the kyphosis. The testes and penis were very small. Both inguinal rings were relaxed. There was a general hyper-reflexia, but there were no pathologic reflexes. The blood pressure was 90 systolic and 68 diastolic. An examination of the blood revealed: Wassermann test, negative; red cells, 4,400,000; differential white cell count, 64 per cent polymorphonuclears, 36 per cent lymphocytes; 70 per cent hemoglobin. The urine was of low specific gravity. The spinal fluid pressure was 50 mm. (actual height in the manometric tube) — a very low reading — with no cells and a negative Wassermann reaction. The basal metabolic rate was —29. The mental status was normal. Examination of the eyes showed the right nerve head with temporal pallor and slight nasal pallor; the margins were distinct; the lamina cribrosa was clearly visible; the vessels and the rest of the fundus were negative; vision was 10/200, with a central scotoma for color. The left eye was essentially the same as the right, but there was less pink in the nasal portion, and vision was 10/30. Examination of the nasopharynx gave negative results. The roentgenogram of the sella showed it to be slightly flattened, and no other abnormality was noted. A diagnosis of a suprasellar neoplasm was made.

Because of the excellent vision, it was decided to treat with deep roentgen rays rather than through operation. We think that in these cases the patients are better treated in a conservative manner, provided a careful watch of the visual function is maintained throughout. Up to the time of discharge from the hospital on Aug. 14, 1930, he received six roentgen treatments; the physical condition remained the same, although the polydipsia and polyuria disappeared.

When he was again examined on October 9, he had had twelve exposures to the roentgen rays. All of the subjective symptoms had disappeared. He complained merely of slight blurring of vision at times, but the field of vision for form had remained normal, and the central scotoma for color, which had been present in the right eye, had disappeared. At the same time the basal metabolic rate had returned to —9 without glandular therapy.

The return of the basal metabolic rate to normal is interesting when considered in the light of the relationship between the pituitary and the thyroid glands. We shall continue with the roentgen therapy and hope to preserve the vision. If, however, we find that there is evidence of advancing atrophy of the optic nerves, we shall be compelled to resort to operative intervention.

#### CASE OF OPHTHALMOPLÉGIA WITH REMISSIONS.

This is a case of ophthalmoplegia with remissions, probably due to a neoplasm or an inflammatory process in the interpeduncular space.

E. S., a woman, aged 50, was admitted to the Mount Sinai Hospital on July 3, 1930, complaining of diplopia and turning-in of the eyes for a year and a half, ptosis of both upper lids and vomiting and headache for the past two months. In December, 1928, following a cold, the eyes had become inflamed. The left eye turned inward, and she saw double. Subsequently, there was palsy of the bilateral external rectus muscle. Two months before admission, she began to have severe frontal headaches. At that time she noticed that the left lid was drooping, and this was soon followed by drooping of the right lid.

Examination revealed that all the muscles of the left eye supplied by the third nerve were paralyzed, while those supplied by the fourth and sixth nerves

were normal; in the right eye all of the muscles were paralyzed, except the superior oblique and the internal rectus which were only slightly affected. There was a complete bilateral iridoplegia. The fundi showed sclerosis of the choroidal vessels with depigmentation; there was marked myopia. Otherwise the neurologic status was normal. Examination of the nose and throat gave negative results. The blood and spinal fluid were normal; there was no increase in the spinal fluid pressure. Roentgen examination of the skull showed erosion of the posterior clinoid processes of the sella turcica and an irregular calcific deposit, about 2 cm. in diameter, directly behind the sella in the midline.

Under antisyphilitic treatment there was some improvement in the condition of the eyes, but after a number of deep roentgen treatments, the improvement was striking. At the time the patient was discharged, there was a slight paralysis of the right internal and external recti, with a return of the reaction of the right pupil to light and in accommodation. The ptosis had cleared up completely. In the left eye, there was considerable improvement in elevating the lid; external rotation was excellent, but other movements were limited. The pupil was fixed.

*Comment.*—This case afforded considerable difficulty in diagnosis. The complete bilateral iridoplegia made us consider the possibility of syphilis or encephalitis. Despite the negative results of the serologic tests for syphilis, the patient was given rather vigorous antisyphilitic treatment, with a resulting improvement in the condition of the eyes, especially in the muscles of the right eye. The presence of calcific deposits posterior to the posterior clinoid process and the erosion of the former induced us, despite the improvement under antisyphilitic treatment, to submit the patient to deep roentgen-ray therapy. She received eight roentgen treatments, with the result that the impairment of the ocular muscles was now restricted almost entirely to the left eye, and even in that eye there has been considerable gain in the power of the muscles.

A case of this kind, showing as it does involvement of the cranial nerves at the base without any signs of intracranial pressure or involvement of the brain stem itself, deserves to be treated conservatively, even though a neoplastic process cannot be definitely excluded. An operation to remove a possible neoplasm in the location involved is not only dangerous to life, but even questionably possible. We do not claim that we have as yet cured this patient. She still complains of subjective symptoms, such as mild headache, occasional dizziness and paresthesia in the distribution of the left fifth nerve, but one must take into account that the patient is of a type who would not feel well with the persistence of any objective symptoms. It is our purpose to continue further deep roentgen-ray treatment.

#### METASTATIC ABSCESS OF THE BRAIN; OPERATION; RECOVERY. DR. IRA COHEN.

In September, 1929, a girl, aged 14, was admitted to the general surgical service at the Mount Sinai Hospital. Two weeks previously she had had a tonsillectomy, followed by daily chills and fever. Five days prior to admission, she began to have pain in the left shoulder. There was nothing of note in the antecedent history. There was fulness of both the supraclavicular and infraclavicular regions, and tenderness over the entire clavicle, most marked over the sternoclavicular articulation. On the day of admission, a subcutaneous abscess over the left clavicle was opened and drained. It did not lead to bone. Following this the temperature remained elevated, ranging between 102 and 104 F. Six days later, a blood culture was reported to contain a gram-negative bacillus. On this day she complained of pain in the thigh, and the femur was found to be tender; a roentgenogram showed evidence of cortical necrosis. A week later, the femur was exposed by operation. The periosteum of the upper and middle thirds was edematous. No pus was seen here, nor was any obtained from four drill holes that were made. A small section of bone sent to the laboratory was reported as showing chronic osteomyelitis. The temperature still remained elevated, reaching 103 F. daily.

*Course.*—On October 5, nineteen days after admission to the hospital, the patient first showed signs of involvement of the central nervous system. On that day she had a convulsion; although it was generalized, the left side was more involved than the right. Following this she showed a left facial weakness as well as some weakness of the left upper extremity. The deep reflexes on the left were more active than on the right, and there was a bilateral Babinski reflex. A blood culture taken at this time grew *Streptococcus viridans*.

It was believed that the patient had a metastatic brain focus, and with the knowledge that they are most often multiple, developments were awaited. During the course of the next five days, the neurologic signs cleared up in large part, although on this day, she had twitchings of the face and hand which lasted for five minutes. The fundi, which were closely observed, remained normal. A few days later, the patient complained of pain in the right ear; this developed into acute purulent otitis media, for which a myringotomy was done about two and a half weeks later. To complicate the picture of the involvement of the ear, a right peripheral facial weakness developed. This cleared up in three weeks. Five weeks after the first generalized convulsion, the patient had another convulsion and was then transferred to the neurological service. The temperature had not been over 100 F. for three weeks, although during this period she had had the ear trouble. In a few days, however, the fundi began to show blurring, the twitchings of the left hand became more frequent, and she vomited. Therefore, on November 26, seven weeks after the first convulsion, it was thought wise to operate for an abscess of the brain which seemed localized in the arm-area in the right hemisphere.

With the patient under local anesthesia, I exposed this area through a defect in the bone approximately 4 cm. in diameter. A thick-walled abscess was found 2 cm. from the surface and drained by a rubber tube. The abscess contained about 30 cc. of thick, foul-smelling pus. The bacteriologic report showed an anaerobic gram-negative bacillus, which would not grow aerobically.

The postoperative course was marked by an increase of the papilledema and of the weakness of the left part of the face and hand, especially the latter, which for a time was completely paralyzed. Although two weeks after the drainage of the abscess, the eyes and the face began to show improvement, the condition of the hand remained stationary. With the help of physiotherapy and reeducation, this also finally came around. The tube was kept in place until January 8, six weeks after the operation. The patient was discharged on March 3, free from symptoms, and has remained well.

*Comment.*—This is an unusual picture of sepsis due to an anaerobic bacillus developing after tonsillectomy, and the occurrence of a solitary abscess in the brain as a metastasis in the course of this sepsis. The formation of a so-called capsule is, in my experience, infrequent with an anaerobic infection; the usual picture is that of a diffuse encephalitis. To the extent that the capsule was formed and that the abscess was solitary, this young woman was fortunate.

#### DISCUSSION

DR. JOSEPH E. JOHNSON KING: Ordinarily, metastatic abscesses are considered hopeless. Here an anaerobic bacillus produced a single, encapsulated, thick-walled abscess, which was well walled off, and Dr. Cohen's capable handling of the case is responsible for the patient being alive. The mere fact that the abscess was encapsulated and single does not necessarily mean that the patient should live; it was rather, the conservative, efficient management of the case that resulted in her being alive today.

DR. LOUIS CASAMAJOR: It surprises me to realize that a metastatic abscess could result in such an extremely good recovery, and besides that, that an abscess containing 30 cc. of pus should have been evacuated and repair have taken place with so little impairment of function. Usually with so much tissue involved, one sees much more residual. Were there any changes in the reflexes to indicate a

real defect in the nervous system such as one could determine by neurologic examination?

DR. IRA COHEN: On examination yesterday there were no residuals. A social worker tells me that the patient is becoming a behavior problem. Whether that is a result of the abscess of the brain or not, I do not know. Before she was taken ill, an intelligence test showed that she was subnormal. She is now rather difficult to manage at home, and whether the abscess and subsequent treatment have increased this I am not prepared to say, but that is the only thing that remains as a residual of the abscess.

THE HISTOGENESIS OF AMYLOID BODIES IN THE CENTRAL NERVOUS SYSTEM.  
(A CONTRIBUTION TO THE PATHOLOGY OF THE OLIGODENDROGLIA.) DR.  
ARMANDO FERRARO and DR. L. A. DAMON (Authors' Abstract).

In the course of a pathologic survey of the Ammon's horns of epileptic persons, we noticed a considerable number of amyloid bodies. These were definitely proved to be amyloid by a typical staining reaction with iodine and also by the reaction to sulphuric acid, methyl violet, Nile-blue sulphate and hematoxylin. We tried to apply to the study of the amyloid body the method of silver impregnation devised to detect microglia and oligodendroglia. We have been successful in studying the morphology of these bodies and in tracing the various steps from their origin to full development.

We believe that the amyloid body is derived from oligodendroglia cells. The first step of the transformation is represented by an acute swelling of the oligodendroglia in which the nucleus first undergoes amyloid degeneration. Gradually the amyloid degeneration involves the whole cytoplasm and a full grown amyloid body is formed. Prolongations can be observed in oligodendroglia cells undergoing an initial stage of transformation into amyloid bodies. Some cells show two or more prolongations. In a further stage of the development of the amyloid body, the prolongations undergo a process of fragmentation, the cell loses its connections with the surrounding elements, and the amyloid body is liberated in the tissue. Collections of three amyloid bodies occur (illustrated by lantern slides), the morphology of which still recall analogous collections in normal oligodendroglia cells.

In conclusion, we think that by the Hortega method we have been able to follow the sequence of events in the production of corpora amylacea, a fact which advocates of various earlier theories of their origin have failed to demonstrate. With the exception of the vague assertion contained in Robertson's textbook of pathology, our contribution represents the only one in the literature dealing with the relationship of oligodendroglia and amyloid bodies.

#### DISCUSSION

DR. JOSEPH H. GLOBUS: A presentation of this sort is perhaps best left undiscussed for the reason that what appears to the observer under the microscope may not appear to one who sees a lantern demonstration of the same slide. Dr. Ferraro made out a rather good case for his idea that amyloid bodies are developed from oligodendroglia, but if one tries to recognize some of the structures he demonstrated as oligodendroglia, difficulties arise in their final identification. Dr. Ferraro showed rounded bodies with long processes at either end. These structures remind one of axis cylinders undergoing globoid swelling. He did not demonstrate in the preparations that the long processes are not axis cylinders that have undergone swelling. In the demonstration he employed material stained by silver methods (and most silver methods are crude, unless they are checked by other methods) to show cells, round or oval with one or more very long process, which he assumes to be oligodendroglia. All these structures, he claims, sooner or later give rise to amyloid bodies. It is an attractive idea, but it is not borne out by the material shown. He showed other cells, which are unquestionably oligodendroglia. That much is true, but he did not show their actual transforma-

tion into amyloid bodies. I could go on quoting examples from what he has shown, but it is unfair to discuss a presentation of this sort unless one has gone over the material carefully. Still, attractive as the conception may appear, it has not convinced me that the amyloid bodies arise from oligodendroglia.

DR. LEO M. DAVIDOFF: I have been a little more fortunate than Dr. Globus in having seen Dr. Ferraro's preparations. If he had seen them I think that he would have been more convinced than he seems to be. I think that Dr. Ferraro did not mean to convey the impression that this is the only origin of amyloid bodies, but as far as he has gone, I think that he has demonstrated as nearly as one can morphologically that amyloid bodies can arise from oligodendroglia.

DR. LOUIS CASAMAJOR: In listening to the paper and seeing Dr. Ferraro's preparations, I think that I shall have to change my views about the corpora amylacea. I have not seen the specimens, but I should like to see them, especially material that has been stained by other methods, for instance, iron-hematoxylin, with which I am most familiar in the study of amyloid bodies. Dr. Ferraro has not had time to give a historical review of the subject; if he had, he would have told us that an origin from the glia has been suggested; and likewise an origin from degeneration of the axis cylinder processes, to which Dr. Globus has called attention. What has always impressed me about corpora amylacea is the tendency of these bodies to gather together in one or more layers immediately under the pia and around the blood vessels, as Alzheimer pointed out, remaining on the neural side of the limiting glia membrane. There may be more than one origin and there may be more than one structure that we call corpora amylacea, for there may be more than one structure that gives this particular group of staining reactions, but the ones I have been inclined to call corpora amylacea seem to be amorphous bodies without any particular form. One gets an impression as if they were made up of layers of concentric rings, very much as an onion, and they tend to gather around the limiting membrane. Alzheimer suggested the origin of these bodies as filtration products, which has always made a particular appeal to me, as though they were filtered out of the tissue fluids by the limiting membrane, which acts as the filter. If they come from the oligodendroglia, as Dr. Ferraro suggests, I wonder how they get through into the region of the blood vessels, and why they do it. The question of there being more than one origin of these bodies is pretty difficult to put on a pathologic basis. Whether there is more than one origin for this group is something that must be left open for discussion; I should like to see some of Dr. Ferraro's material in order to prove to myself that corpora amylacea may be of glia nucleus origin.

DR. ARMANDO FERRARO: Dr. Globus made the remark that it was not fair to discuss my paper unless the slides were seen. I agree with his statement, but Dr. Globus should have stopped right there, as I do not see how he can logically reach the conclusion that my demonstration has not convinced him.

If Dr. Globus had listened to my paper, he would have heard a statement in which I said that we have not been able, even by the use of specific methods, to encounter other structures which may suggest a transformation into amyloid bodies. We have used a variety of staining controls, for instance, the Nissl for nerve cells, the Cajal for astrocytes and the Bielschowsky for neurofibrils, and have failed to see the transformation of other elements into amyloid bodies. This settles Dr. Globus' claim that the amyloid bodies I have shown might be swollen axis cylinders.

I have to add now that Dr. Uyematsu, professor of psychiatry in Tokio, who is particularly acquainted with the subject of amyloid bodies, having written a paper on their origin from swelling of the prolongations of the astrocytes, has carefully studied our slides. He was kind enough to spend a couple of hours in our laboratory studying them, and at the end of his investigation was glad to tell us that we were right. Such a statement coming from so competent a person is certainly gratifying.

We have shown not only round bodies with prolongations, but also cellular elements, that is, oligodendroglia, on the morphology of which no doubt can be cast, as can be proved by the slide projected previous to the last. It is in the center of oligodendroglia cells that we have found amyloid bodies, the origin of which is an amyloid degeneration of the nucleus. Our contention was checked by staining successive sections respectively with the amyloid stains and with silver impregnation.

It is true, as Dr. Casamajor pointed out, that there have been numerous theories concerning the origin of amyloid bodies, among which are the neurogenic theory, the gliogenic theory, the lymphogenic theory, the hematogenic theory and the theory that considers the amyloid bodies as postmortem changes. We have gone over the possibilities of most of them and have found no convincing proof in their support. As to the origin of amyloid bodies from oligodendroglia, the only mention we found in the literature is the vague assertion in Ford Robertson's textbook on pathology in which he mentions the transformation of the mesoglia into scavenger cells and amyloid bodies. No description or pictures, however, illustrate such a statement.

PROBLEMS IN THE DEVELOPMENT OF THE NERVOUS SYSTEM. DR. S. R. DETWILER.

Since the classic researches of Harrison (*J. Exper. Zool.* **4**:239, 1907; **9**:787, 1910) on the genesis of the nerve fiber and its growth in vitro, many lines of investigation have been initiated with a view of studying the forces that bring about the development of normal architecture in the central and peripheral nervous systems. By reason of the complexities of development and of the limitations of the experimental method, our knowledge of these forces lies little beyond the theoretical stage. By direct observations on developing embryos, through studies on regeneration, and, in more recent years, by the methods of transplantation and explantation, many interesting and important facts have been discovered. From these facts, suggestive theories have taken form. Among them may be cited the original neurotropism theory of Cajal (*Cellule* **9**:119, 1892), the theory of neurobiotaxis of Kappers (*J. Comp. Neurol.* **27**:261, 1917; *Brain* **44**:125, 1921), embodying the interesting stimulogeneous fibrillation concept of Bok (*Folia neuro-biol.* **9**:475, 1915), and more recently the gradient hypothesis of Child (*The Origin and Development of the Nervous System*, Chicago, Chicago Univ. Press, 1921, pp. 1-296). Tello (*Vortr. u. Aufs. Entwicklungsmechr. d. Organ.* **33**:1, 1923) has given a general account of the different neurotropism theories, and his paper contains an excellent account of many important observations that bear on various aspects of the subject.

During recent years, the method of grafting embryonic tissue has been employed extensively as a means of studying morphogenesis and developmental physiology in the nervous system. In this connection the transplantation of the rudiments of the embryonic limb has been of interest in demonstrating certain characteristic developmental responses of the growing peripheral nerves to alterations at the periphery (*J. Exper. Zool.* **31**:117, 1920). These experiments have shown that if the rudiment of the forelimb of the salamander embryo is excised and reimplanted at short distances from the normal site (from two to four body segments), the original brachial nerves will grow out of their normal pathways to make connection with the developing appendage. These and other experiments (*J. Exper. Zool.* **51**:1, 1928) have demonstrated that the limb exerts an attractive influence on the developing brachial nerves, and indicate, as well, that there is nothing specific in the attraction, for other organs (e. g., nasal placode) grafted to the same position may exert a similar attraction.

When supernumerary limbs are grafted close to the normal limb, the brachial nerves may become redistributed to both appendages—in which cases synchronous movements occur in the homologous muscles of the two limbs. Such movements do not depend on the distribution of the same nerve to both limbs. A super-

numerary limb that receives only one brachial nerve, or even a branch, may exhibit complete coordinated function in its various muscle groups. In such cases the movements of the muscles of the limb are again entirely synchronous with the corresponding muscles of the orthotopic limb (J. Comp. Neurol. **38**:461, 1925; **47**:427, 1929). The same observations were made by Weiss, who endeavored to account for this striking phenomenon by a new concept of reflex activity termed the "resonance theory" (Ergebn. d. Biol. **3**:1, 1928).

Experiments on nerve section have shown that when supernumerary limbs exhibit coordinated movements, their nerve supply must come, at least in part, from the brachial region of the cord. When this ensues, complete movements in the various muscle groups may be effected through only a small branch of the brachial nerve.

Regulation of the motor nerve to peripheral overloading (extra limbs) is accomplished by repeated division of the axis cylinders and not by the proliferation and differentiation of more motor horn cells. On the other hand, the sensory ganglia respond strikingly to alterations in the peripheral field. Hypoplasia in the sensory ganglia of the brachial nerves follows the excision of a limb, whereas hyperplasia occurs in those ganglia that are connected with grafted limbs (Proc. Nat. Acad. Sc. **6**:695, 1920). Experiments involving a known quantity of skin and muscle reduction in the embryo have made it possible to estimate the proportion of ganglion cells that develop in relation to areas of skin and to volume of muscle (J. Exper. Zool. **45**:399, 1926; **48**:1, 1927). In addition to this functional relation between the volume of muscle and the number of cells that develop in the ganglia, it has been shown in recent experiments by Lehmann (J. Exper. Zool. **49**:93, 1927) and by me (unpublished results) that orderly segmentation of the spinal ganglia is subservient to a normal segmentation of the mesoderm. Any disturbances in the latter are accompanied by abnormal segmentation of the neural crest cells.

The failure of the motor areas of the spinal cord to hyperplase in response to increased requirements at the periphery, such as occurs in the sensory ganglia, has suggested that the factors responsible for the production of a given number of motor neurons at any level of the spinal cord are primarily intrinsic, rather than extrinsic, to the central nervous system. Many experiments involving the transplantation of various segments of the spinal cord from one level to another have supported this view (J. Exper. Zool. **37**:339, 1923; Quart. Rev. Biol. **1**:61, 1926). When the brachial region of the cord (third, fourth and fifth segments) is excised and is replaced by a unit of cord comprising the seventh, eighth and ninth segments, the latter develop as many cells in their new location as did the original brachial segments, regardless of whether a developing limb is present or absent (Anat. Rec. **27**:64, 1924). That the number of cells developing in the more anterior end of the cord is influenced by higher centers has been shown experimentally by me (J. Exper. Zool. **41**:293, 1925) and confirmed by Nicholas (Arch. f. Entwickl.-lingsmech. d. Organ. **118**:78, 1929).

The production of cells in various spinal segments when removed from the influences of the remainder of the central nervous system, by grafting to an isolated position, has recently been studied by Severinghaus (J. Comp. Neurol. **51**:237, 1930).

Experiments of a similar type have been performed by Rogers (unpublished results), who obtained dual innervation to the limbs from both normal and grafted cords.

Many other experiments, too numerous to cite, have been carried out on the developing embryo, with results that have given many new concepts regarding the developmental physiology of the nervous system and sense organs.

#### DISCUSSION

DR. H. D. SENIOR: One of the most remarkable things that we have learned from Dr. Detwiler and his coworkers is the extreme adaptability and longsufferingness of the amphibian larva. It is a great feat for Dr. Detwiler to show that overloading by the grafting of a new limb will cause hyperplasia in the ganglia

on the dorsal root of the nerve, without an increase in the motor neurons in the corresponding segments of the central nervous system. That result is perfectly clearcut, and Dr. Detwiler has referred to the fact that he has shown that hyperplasia of the neurons in the central nervous system can be brought about only by changes in the central nervous system and not by peripheral overloading by means of transplanting an extra limb. To go on as he has done, and make arrangements by which there shall be less skin in comparison to the muscles, and to produce the contrary result by denuding, so to speak, the animal's muscles on one side, seems to me truly remarkable. I have no doubt that Dr. Detwiler will go into details about his experiments at a later time. I hope that he will.

I have been particularly interested in a question that used to be quite acute, although one does not hear very much about it now. I refer to the question of whether the backgrowth, which Dr. Detwiler said occurs in the brachial plexus in cases in which the limb is moved to a more caudal part of the body, is due to a specific attraction by the limb for the nerves of the limb as such, or whether it is simply a response to an area of local increased peripheral growth. Dr. Detwiler is a very careful worker, and it seems to me that he is sometimes a bit too modest. The question was raised first in his own experiments of 1920, and as late as 1928 he raised it again. He states it like this: "Is the attraction which these limb-buds (he was referring to a case in which he transferred a limb-bud to a different position in such a way as to have both the transplanted limb-bud and the regenerated one) exert upon growing nerves an expression of developmental relationship, or is the atypical nerve growth to be regarded only as a growth response towards a center exerting high physiological activity?" That seems to me a very fundamental question. Before this work was started I think that we would have said that the limb was the natural end-organ of the brachial plexus. Now that idea seems to have been entirely exploded, but I should like to ask Dr. Detwiler when he thinks that it was exploded. It seems to me that he had pretty well disposed of the idea before the year 1928 in which he wrote that paper. After having removed the limb-bud in an early stage, called the tail-bud stage, as he did in 1922, there was no local limb for the nerves to grow into, so the third, fourth and fifth nerves, which normally grow into the limb, simply went out to the periphery. When the nerves had grown out, Dr. Detwiler then transplanted another limb about four segments caudal to the original position, and the local nerves entered it. Nerves posterior to the proper brachial nerves (such as the sixth, seventh and eighth, depending on position) now formed a plexus and grew into the limb. The interpretation of this is open to doubt. In this case the transplanted limb exerted its influence after the brachial nerves had grown out, with no limb for them to grow into. Did the failure of the brachial nerves to reach the new limb depend on their previous fulfilment of their destiny (so to speak) or on the time limit of their ability to grow? This question seems to be partly answered by Dr. Detwiler's experiment of 1924, in which he transplanted a limb about four segments caudally, leaving the wound in such a state that regeneration would be likely to follow. In the cases in which regeneration occurred, the transplanted limb received the fifth, sixth and seventh nerves (with or without the eighth, according to position). Here again there is a time factor, but the regenerated limb received the third and fourth nerves in spite of the lateness of its appearance. Although perhaps not quite conclusive, the two experiments together appear to me to indicate that it is the vigor of local growth rather than the specific attraction of the nerves of a limb for those of another limb that calls forth nerve growth. In 1928, when Dr. Detwiler called attention to the question again, he transplanted the olfactory placode and the optic cup. The limb was removed, and, four or five segments back, the olfactory placode and the optic cup were transplanted, and the brachial nerves grew back toward them, just as they would have grown back to a transplanted limb, but made no actual connection. There was nothing very much to make a connection with. These are not end-organs. They are full of neuroblasts, and they themselves have axons to dispose of, and it seems to me that it is rather a complicated case. I

would like to ask Dr. Detwiler if it would not have been as well to transplant into that position a mandible from another animal, or even a hind limb? I do not know what the objection to a hind limb is, but if a hind limb is objectionable, would not the mandible have done? An objective of another kind, I think, is open to the tail-bud grafts which form part of the same series of experiments.

It seems to me that the question was definitely settled in Dr. Detwiler's later experiments, which he reported in 1930, in which the forelimb was transplanted to the head. In this case the limb received branches from the local ganglia, and also made connections with the nerves of the medulla. Here was a limb which exerted just as much attraction on the cranial nerves as it could have exerted on any of the nerves of the body, either in the brachial region or elsewhere. It seems to me that that shows definitely that there is nothing specific between the brachial nerves and the limb-bud. When the limb-bud is transplanted, it calls forth growth of the local nerves, whatever they may be.

I, of course, am subject to correction in this matter, for I feel that experimentalists are great discoverers of fallacies. They discuss the matter between themselves, and their work has to be very clearcut and their experiments perfectly suited to the object for which they are planned. But, I also feel that to an ordinary person like myself and to most who are not engaged in experimental work, it would be instructive if Dr. Detwiler would tell us when this nonspecificity was definitely proved. I personally have the impression that he proved it before performing the experiment of transplanting olfactory placodes.

Another thing that has interested me is the question of symmetrical movements on the two sides. In order to get symmetrical movements on two sides, Dr. Detwiler has shown that a transplanted limb needs to have at least one nerve belonging to the proper brachial set. The nerve in point is usually the fifth nerve, and Dr. Detwiler has shown that if the fifth nerve going to a transplanted limb is subsequently cut, symmetrical movements cease. Looking at the problem from the surface, it would seem that in order to secure symmetrical movements with the combination of the fifth nerve and two nerves that do not ordinarily go to the limb (the sixth and seventh), the fifth nerve must be represented in all of the muscles of the limb.

DR. GEORGE V. N. DEARBORN: I think that Professor Detwiler is to be greatly congratulated on making a contribution to the biologic tendency, of late found in so many different directions, proving that the nervous systems of animals in some way or other are adaptable to "function," purpose and individuality without any assignable limit. It looks as if the animal were inherently a center of activity, of purposeful behavior, with specific things to do, something to accomplish, and that the animal should properly be evaluated from that point of view rather than from its structural, materialistic, anatomic aspect. The structure of muscles, of glands, of nerves and of bones seems to be adaptable to usefulness without known limits. There are implications here broader than the anatomic matter of morphology. The implications, of course, are that function, purpose, is the fundamental thing, and that by physical forces yet to be defined that purpose is to be carried out under the most adverse and, apparently, sometimes "impossible" circumstances. To some of us, that philosophic implication is of tremendous import for the deeper, modern understanding of things. It gives us another sanction, and one above the ordinary, for every kind of scientific research, and in this case this fine study gives us another dramatically interesting link, so to speak, in the chain that is so rapidly confirming monism and drawing pure science nearer to the philosophy of our very existence. I say again that I think Professor Detwiler is to be congratulated on adding one more and a very large element to this progress, obvious of late in so many different ways.

DR. E. D. FRIEDMAN: Would Dr. Detwiler bring the results of his experiments into line with Kappers' theory of neurobiotaxis? Was the enlargement of the posterior root ganglia due to an actual increase in the number of cells or to an increase in the size of the cells already present?

DR. ARMANDO FERRARO: I would ask the same question regarding the size of the nerve cells. As a result of his experiments, Dr. Detwiler found hyperplasia of the nerve cells in the spinal ganglia as an explanation for the increase in size of the ganglia. This statement contrasts with the results of Levi and Terni who have been working on the same subject, and who have found that under the same circumstances there is an increase in the size of the nerve cells themselves. Concerning the relationship between the surface of the body and the size of the nerve cells, there is even a law known as Levi's law, which is that the perennial elements (nerve cells, nerve fibers and muscular fibers) are directly proportionate in volume to the volume of the body.

I ask this question also because of some experiments that I performed about ten years ago by grafting together several motor roots, more precisely, the seventh lumbar root of a dog onto the sixth, and the sixth onto the fifth. A motor paralysis followed the section of the sixth and the seventh, and later a return of function was established in the peripheral territory of the three roots mentioned. It is natural to assume that the group of nerve cells that gives origin to the fifth lumbar root had supplied the motor power for the peripheral territory of the sixth and seventh lumbar roots. I should like to ask Dr. Detwiler if he has any suggestions to offer as to the mechanism of this increased function of one group of cells. Does it take place through an actual increase in the number of nerve cells, even considering the adult animal? Does it take place through an actual increase only in the size of the nerve cells, or does it take place through an increase in the number and size of the nerve fibers of the motor root?

DR. MICHAEL OSNATO: I wish to thank Dr. Detwiler for coming here. In my opinion there are implications in this work of tremendous practical importance. One occurs to me in line with the question that Dr. Ferraro has just asked. It seems to me that the question does not concern the size or number of cells in the spinal cord. I think that most neurologists in the last generation have missed the mark by going too far up in the central nervous system for the answers to the questions that they are asking in connection with movement. The importance of the spinal cord as a segmental unit in movement, it seems to me, has been neglected. One is too apt to think, thoughtlessly, of the spinal cord in a motor way as simply the anterior horn cells in relation to the corticospinal tracts, forgetting that there are many extremely important mechanisms that are entirely extrapyramidal, representing systems that are much older. The oldest of all is the segment of the spinal cord, representing connections with cord patterns that must be, *per se*, of immense importance for movement. In the experiments of Dr. Detwiler, we all saw that homologous, coordinated movements occurred in the grafted limbs because of the preservation of the fifth brachial nerve, representative of the segmental cord unit, and that when this was missing, an inefficient, economically useless limb resulted. One lesson, I think, to be drawn from this tremendously important piece of work is that in the past we have slighted too much the importance of segments of the spinal cord as units in the execution of pattern movements, and that we have made the mistake of looking for the site of the localization of these functions exclusively in the higher segments of the central nervous system. I think that this is one of the many implications that one may draw from this work. On behalf of the Section, I again wish to thank Professor Detwiler for presenting it.

DR. LOUIS CASAMAJOR: It would be a temerity for me to attempt to discuss such a presentation. Dr. Detwiler makes us feel almost as though we were being taken behind the scenes in the workshop of a creator. There were one or two points that interested me especially, although I do not expect Dr. Detwiler to answer my questions, because he never does, as he says he does not know the answers. One of the interesting points he brought out is the lack of increase in the anterior horn cells that supply these newly created limbs in spite of the enormously increased number of the spinal ganglion cells. I assume that those spinal ganglion cells are all sensory, although if Dr. Detwiler were to tell me that he grew motor cells in the spinal ganglia I should be perfectly willing to

believe it after what I have seen that he is able to grow elsewhere. But assuming that these are all sensory, one would tend to think that in the formation of these limb-buds and functioning limbs there is a greater necessity for an increased amount of sensation, not only in the skin but much more important, in the muscles, than there is of pure motor cell function. A certain number of motor cells in a spinal segment can apparently supply almost any number of muscles that do almost any number of things, but in order for them to do these various things they need to have a much greater sensory component than if there were less musculature to be supplied. Whether one can draw any conclusions from that as to the importance of the sensory part of motion I do not know. Maybe Dr. Detwiler will tell us. I could draw a lot of conclusions, but I am equally sure that they would be wrong.

DR. S. R. DETWILER: There appears to be something fundamentally different between the development of primary sensory and motor neurons. Changes in the peripheral territory (skin and muscle) are accompanied by a definite developmental response on the part of the sensory ganglia. Reduction of the peripheral territory is accompanied by a marked hypoplastic development of the spinal ganglion neurons. Increase of the peripheral territory (brought about by the addition of limbs) is followed by hyperplastic development of these neurons. The alterations in the size of the ganglia as a whole are primarily the result of alterations in the numbers of cells and not of changes in the size of the cells.

There is something associated with the ingrowth of peripheral axons into the central nervous system which effects the cellular production therein.

When the entering optic nerve of a heterotopically grafted eye penetrates nerve centers, a hyperplasia of the cells usually occurs. The fusion of several nasal placodes, whereby a large olfactory nerve is produced, is usually followed by hyperplasia in the olfactory portion of the hemisphere. In heteroplastic eye grafts, in which large eyes develop in place of small ones, the entrance of the large optic nerve into the midbrain has been shown to produce hyperplasia.

That spinal nerves may be attracted in their growth to their end-organs appears to be a fact from the experiments cited. The evidence appears to support the view that there may not be anything specific in this attraction. The fact that any spinal or cranial nerve can be made to supply a grafted limb is an argument in favor of the lack of specificity between the nerves and the muscles in a limb.

These experiments are of interest in connection with Kapper's theory of neuro-biotaxis and with Bok's stimulogenous fibrillation concept. The actual influence, however, of the development of galvanic fields on the growth of nerves, cellular proliferation and differentiation can only be estimated critically as more experimental evidence is produced.

## Book Reviews

DIE "UNFALL- (KRIEGS-) NEUROSE." Number 13. Edited by PROFESSOR MARTINECK. Price, 4.20 marks. Pp. 144. Berlin: Reimer Hobbing, 1929.

This book contains a symposium on the war and traumatic neuroses, setting forth the opinions of leading German authorities, and is used for purposes of instruction by the German Department of Labor, especially by physicians engaged in the handling of compensation cases. The executive officer of the German Department of Labor requested Kronfeld, Leppmann, Jozsman, Stier, Hoche, Wilmanns and Knoll to discuss current medical opinion as regards the question of hysteria and to express their convictions or attitude toward the following questions:

Are persons with nervous manifestations (hereafter interpreted by the German Department of Labor always as reactive, neurotic and not organically determined symptoms) eligible for compensation: (1) when, after some external accident, the symptoms become manifest for the first time many years later; (2) when they appear once again (in the same, a similar or a completely different way) after prolonged absence or extensive improvement; (3) when, after remaining stationary for many years, they become worse; (4) when, compensation once awarded, they still continue to exist unchanged for many years?

Chapter 2 comprises a series of addresses by the various authorities mentioned on the subject in point.

DR. ARTHUR KRONFELD

Kronfeld discusses his observations on the structure of the so-called traumatic neuroses. By the concept "traumatic neurosis" is understood, exclusively, cases in which an accident has induced mental elaborations based on an alleged injury. The psychologic structure of the traumatic neurosis is beyond question.

Prevailing scientific opinion observes a certain uniformity in the mental elaboration of these neuroses. It discovers certain wishes, desires or demands which are aimed at obtaining advantages and compensation from the traumatic event experienced, and which act as a constantly recurring fixative factor through which the traumatic experience undergoes a permanent mental elaboration in the sense that the person injured feels that he has suffered an alleged injury. One is dealing with a volitional attitude, not fully conscious, the object of which is to gain from the traumatic event those legal advantages which are permitted by the social legislation associated with general insurance, accident insurance and the care of persons injured in war.

This prevailing medical opinion has been carried over into the decisions of the German Workingmen's Insurance Department. Other views prevalent in the medical profession are ignored. Lack of knowledge on the part of physicians concerning the prevailing views on the nature of the neuroses is solely responsible for the diversity of expert opinions. Whoever comes in contact with these cases, not only as a psychiatric expert but as a psychotherapist, and whoever regards the so-called traumatic neuroses as essentially in no way different from neuroses in general will harbor certain doubts about the tenability of this prevailing view.

To the latter, the great advance lies in a spreading of the psychologic understanding of the nervous elaborations following accidents. He will admit that the majority of traumatic and war neuroses that come before medical experts for compensation belong to the type mentioned. For the purposes of expert testimony, the prevailing view is adequate and sifts out an important determinant of the neuroses. The psychologic and psychophysical situation in the traumatic case, however, is not exhaustively understood.

The prevailing view on the nature of these neuroses, however, does not hold good in a minority of cases. One must not consider them exceptional cases merely because they are in the minority. The number is small among those injured in war. They belong to a relatively one-sided group of persons, not only as to age and sex, but also according to the type and peculiarity of the accident and the psychic and psychophysical make-up of the person before the accident. They are more frequent in persons who in civil life or in the performance of their work showed nervous symptoms after accidents.

There are three points on which the prevailing attitude draws too sweeping generalizations: (1) regarding the equivalence of the mental elaborations following accidents and wishful or covetous ideas; (2) regarding the assertion that it is characteristic of all other affective or emotional reactions to outside experiences that they subside rapidly; (3) with respect to the exclusion of nervous and mental elaborations following accident from the concept of disease.

As regards the first point, it is true that a great number of those who express demands for compensation after an accident do so predominately or exclusively under the pressure of conscious or unconscious wish-tendencies. If it were not for present social legislation, the mental attitude of large groups would not be determined in this direction. The fact, however, that one cannot regard the complaints and symptoms without further ado as simulation indicates that commonplace psychology does not exhaust the situation. Psychology of this type, which the medical expert attaches to his patients, is to be regarded solely as the product of the mentality created in the trauma-expert by social legislation, as is the case with the person injured in an accident when he egoistically imposes on this legislation. It is affectively determined and not based on objective investigation.

As proof for this contention there is the experience that the so-called traumatic neuroses, in contrast to all other diseases, can be cured by money or by granting compensation.

Kronfeld believes that this assertion is not backed by that kind of statistical certainty which is demanded by a generalization of this character. The few statistics that are available do not lend unobjectionable support to the assertion. Kronfeld believes that money or other material advantages can favor recovery in other diseases too, not only the nonnervous ones, but those of organic character.

It has been alleged, too, that in persons not insured or eligible for compensation who experience an accident all nervous manifestations of a chronic type are absent. This generalization is, however, erroneous. It is usually corroborated by pointing to injuries received in fencing or other sports. In the latter instance, the type of person involved is different, in a psychologic respect, from the one in a case of trauma. The element of surprise, fright and defenselessness to vital danger is absent. Moreover, in sport the person realizes beforehand that for the sake of pleasure he exposes himself to danger, and his mental state prior to the accident is therefore different. To be sure, the sequelae of trauma of a chronic nervous type are rarely observed in persons who are not insured. It is readily understood, too, why medical or insurance experts see so few cases of persons of this type; they have no reason to examine them. Neurologists and psychotherapists, however, see them.

In regard to the second point, it is claimed that all the nervous sequelae of trauma, which are not fixed by covetous desires, vanish after a short time. This is only partially correct and sometimes erroneous. In part, it assumes the solution of a question concerning which there is insufficient knowledge. Lack of knowledge is confined particularly to cases in which the injury was not solely limited to the effect of an experience, but was simultaneously associated with vague organic sequelae in the nature of concussion or marked injury. This also applies to cases in which the patients were organically sick before the accident and suffered aggravation as a result of it; also to cases in which severe vasomotor conditions followed the accident and did not clear up. It is difficult to understand how angiospasm, chronic edema, congestion on bending forward and intolerance to alcohol could possibly represent the expression of covetous ideas.

In order actually to measure the exact degree of traumatic effect and to draw conclusions regarding its proper duration, the premorbid situation of every case must be evaluated without prematurely resorting to the assistance of the "wish-idea."

The prevailing theory displays a certain amount of contradiction by the fact that on the one hand it maintains that in the mental elaborations following an accident one is not dealing with disease, but with a psychologic reaction with "wish-ideas," and, on the other, that the person who reacts in this manner is a diseased personality to begin with—the traumatic neurosis is only a manifestation of a psychopathic anlage, and the latter is the disease and not the former. Wish-ideas may also be present in a healthy person. But the healthy person cannot express his wish-ideas in the form of a neurosis. He can simulate. Not even the most ardent adherents of the prevailing theory have ever maintained that the thousands of persons with "traumatic neuroses" are merely simulators. The notion of psychopathic anlage is used to straddle this difficulty. Often one can actually show that the patient in the traumatic case was normal in a social and psychologic sense before the advent of the accident. Psychopathic mechanisms spread far beyond the realm of psychopathy and occur with more or less latency among healthy persons.

Recent investigations into the psychology of the neuroses, moreover, show that it is not always necessary to have a psychopathic anlage to develop a neurosis. The construction of the traumatic neurosis is no different from that of the neuroses in general. Without going into the structural theory too closely, three factors of importance are pointed out: (a) The affective-dynamic and psychophysical situation which preceded the traumatic event. (b) The vital effect of trauma. Every neurosis, not only the traumatic neurosis, is built on a psychic trauma. Vital conflicts, both internal and external, function in this manner. The traumatic nature of such exciting factors need not be experienced as such, but makes itself manifest at times solely by its further intrapsychic effects. In accidents this makes itself manifest acutely and strongly, not only as fright but also as surprise, as vital danger against which the subject is defenseless. The accident as such, despite its elementary character, is variously colored, depending on the premorbid situation and its patterns of reactivity. (c) The purposive, prospective factor. This is inherent not only in hysterical reactions, but in every neurotic reaction. In it become realized the urge for flight and for security, for defense and increased self-interest as well as all those instinctive needs which had to be maintained before the accident occurred. Wish-tendencies become realized; feelings of guilt are overcompensated and experienced as self-pity.

The fright reaction as a rule disappears in a few days, and when this is not the case other factors are at play.

Regarding the third point, if the traumatic neuroses do not differ from other neuroses, their elimination from the concept of disease implies the removal of all other neuroses from the concept of disease. This does not do justice to the medicobiologic aspects and gives preference to the pathologico-anatomic concept of disease. The insistence on a pathologico-anatomic criterion for disease contradicts all tendencies of modern medicine. It is possible to use psychotherapy in traumatic neuroses with no less fertile results than psychotherapy in neuroses generally.

All agree that it is untrue that the occurrence of the accident is generally the cause of the neurosis. But the opposite view, by virtue of its generality, is also erroneous. From the causal standpoint, the accident is important from the purely affective influence of the event. One must evaluate the relationship between the accident and the premorbid mental and psychophysical total situation. Every case requires careful analysis; this cannot be estimated by a single examination, as is now the custom.

Kronfeld answers the four questions cited at the beginning of this article as follows: (1) No. (2) No. (3) No. (4) To answer this difficult question the following possibilities must be considered: (a) Cure is hindered by a conflict producing situations that are accompanied by a maintenance of symptom pro-

duction; these depend on special conditions in the life of the neurotic person and his neurotic attitude toward them. (b) The antecedent proceedings associated with compensation and their production of mental excitement tend to assist in maintaining the neurosis; or worry, poverty, self-preservative inclinations and covetous ideas can aim toward need for further compensation. Both series of possibilities cannot be brought into causal relationship with the accident.

DR. FRIEDRICH LEPPMANN

1. Even if manifested as physical disorder, the neuroses in the narrower sense are the expression of abnormal mental reactions.

2. The greatest number of the chronic, so-called war or traumatic neuroses, particularly of the hysterical type, do not arise as a direct reaction to war injury or accident, but as the result of subsequent wish-determined mental elaborations of these events.

3. What is stated in 2 does not hold without further consideration for a much smaller number of clinically different neurotic developments following war injury or accident: obsessional neuroses, anxiety neuroses, pure depressions and actual hypochondria.

4. The commotion neuroses are not genuine neuroses, but are the organic sequelae of concussion of the brain. They cannot always be differentiated in one examination from purely mental reactions.

5. The same holds true for a series of "pseudo-hysterical" and "pseudo-neurasthenic" conditions of organic origin. A typical example is the nervous complaints after epidemic encephalitis.

6. The existence of a neurosis does not always imply the presence of an essential congenital inadequacy of the personality (psychopathy).

7. The effects of war, with its possibilities for prolonged unhealthy influences and accumulated mental and physical trauma, formed good soil on which to create a neurotic capacity without important psychopathic anlage.

8. When the impaired efficiency as a result of primary organic sequelae of war or accident robs the injured person of his source of existence from time to time and also impedes his rehabilitation, then the efficiency in consequence of poverty and worry may continue at a reduced level after subsidence of the direct organic sequelae of war and accident (through insufficient nourishment, insomnia, etc.).

9. The considerations in 8 account partly for the rareness of war and accident neuroses in persons who following injury do not work full time after a short vacation and who are protected from business worries (prisoners of war, students, sportsmen). The cure of a neurosis through payment of money, which tides the injured person over a critical economic situation and thereby makes full recovery possible, can in part be explained in this way.

Leppmann answers the special questions relative to the genuine neuroses as follows: (1) No, because it is not conceivable that a mental reaction following such an accident could become effective only years later. (2) No. The probability that one is dealing with reactions to new experiences is justified from general knowledge even if one is unable to demonstrate these new experiences in the individual case. (3) No, because the neurosis does not represent a disease process which progresses on the basis of a primary disease-producing cause, but rather a mental reaction which tends to recede, as a rule, through a paling of the primary experience. (4) If the neurosis, once compensated, continues to exist unchanged for many years, it is assumed that the injury itself or a chronically effective mental conflict has prevented a cure. But this assumption cannot be used as a schematically applied rule which in itself would form the basis for refusing compensation that was awarded on account of the same neurosis. In such cases, one must determine with particular care what data can be obtained regarding the habits and industry of the annuitant; his general physical status is to be considered as well as his mental attitude.

The difficulties lie in three directions: not every mental reaction to an accident is to be looked on as equivalent to a hysterical reaction; not every hysterical or psychogenic-appearing symptom picture actually represents a hysterical reaction, and many a real hysterical reaction is merely superimposed on an organic injury that is recognized with difficulty. In theory, nowadays, one separates sharply from the hysterical reactions those organic symptoms which are the genuine sequelae of injury to the skull or cerebral concussion, as they were known long before the theory of the traumatic neurosis existed, to wit: headache, vertigo, specks before the eyes, change of personality (ill humor, irritability, memory disorder and increased fatigability). In practice this is not so easy.

Negative observations do not justify the assumption that one is dealing with a hysterical reaction.

DR. PAUL JOSZMANN

Nowadays, the old theory of the material, organic basis of neurotic conditions following accidents, the prototype of which was Oppenheim's theory, is hardly encountered in discussions. A relative agreement of opinion prevails regarding the reactive, psychologically understandable character of the manifestations in question. Differences of opinion occur only in evaluating the pathogenesis, i.e., in lining up the causal relationships.

In the "compensation-neuroses," one will find an attitude which does not differ fundamentally from that found in other psychogenic, hysterical, reactive conditions, except that their impelling motives prove to be wish-attitudes, protective tendencies, etc.

Joszmann's attitude toward the four questions is: (1) No. Causal relationship is neither possible clinically nor theoretically. (2) No. (3) No, because other factors, outside of the original pathogenic ones, are at play. (4) It will depend on the peculiarities of the individual case to what extent the medical expert will recommend cessation of compensation, gradual reduction of compensation or further compensation to the proper authorities. One should evaluate the suggestive effect of morbid ideas which have remained fixed for many years, and the probability of social rehabilitation and return to work.

DR. E. STIER

Modern anatomy and physiology of the nervous system show nothing that would support Oppenheim's theory on the anatomic determination of hysterical and neurotic conditions. Continuation of the discussion, whether mental and hysterical reactions in particular are disease or not, will not help to bring about understanding. If it were possible to answer this question with a yes or a no, then one would have discovered a very comfortable formula with which jurists and legal officials could reach a decision. Unfortunately this is not the case. One must realize that nature does not make jumps. The transitions from a person who is unquestionably sick to one who is definitely not sick are just as insensible or flowing as, in ethics, the transition from the concept of good to the concept of bad. All transitional phases actually occur and are the rule.

The problem of the medical expert is not to determine whether or not disease exists, whether one is dealing with the reaction of an average person or of a psychopathic individual, but rather to study and size up the total personality of the person to be examined in his physical and mental aspects and then to demonstrate how the unusual condition in question and the peculiar reaction can be explained as the result of the reaction of special experiences against a definite psychophysical organism. The difficulty of this task in every new case is usually underestimated.

Ethical or even politico-economic points of view should not be injected into expert testimony. As psychiatrists, we can only regret that the Workingmen's Insurance Department insists on separating conscious from unconscious wishes. In this instance, one can never say "either . . . or," but always "more or less."

It is generally recognized that in what is known as an hysterical state one is not dealing with a biologically tangible disease, but with mental reactions

that can be understood only psychologically. All agree that Bonhoeffer was correct when he spoke of "volitional tendencies," which are at the bottom of the reactions in question. As a rule, though not always, the volitional tendency is merely a wish to be considered ill in order to be withdrawn from situations regarded as unbearable or to obtain improvement of the present situation.

The directors of the German railroads, in Berlin, report that cases rarely occur in which a severe or permanent impairment of nervous or mental health followed a pure fright-producing accident. Almost without exception a satisfactory agreement and rapid subsidence of the reaction is quickly attained nowadays.

The Berlin Street Car and Omnibus Company, which in 1928 had no less than 2,386 requests for damages following accidents, report that in contrast to former times cases of so-called traumatic neurosis were hardly ever observed. The hopeless trembling and jerking neurotic patients, who stand aloof from every form of work, are no longer observed.

One of the largest vocational bureaus reports that in the Central German District cases of traumatic neurosis practically never occur now, while in the Ruhr district conditions prevail somewhat as before. The director of the vocational bureau believes (and probably correctly) that the reason for this lies in the fact that in Cologne and Düsseldorf some medical experts who are recognized by the courts still cling to old points of view, and the courts tend to decide accordingly.

The Post Office of Berlin was the earliest to accept deliberately the modern scientific attitude. The result was overwhelming. Indeed, not only were the countless old cases finally adjusted, but new cases of "fright neurosis" or "telephone accidents" at once became less frequent, and in recent years, particularly, are no longer observed.

Stier answers the first three questions of the questionnaire concerning the allowance of compensation for nervous manifestations in the negative. In answer to question 4, he says that among an enormous number of cases of damage he has not seen a single one in which hysterical reactions were present for more than ten years without pause or in unchanged form. Indeed, it was not observed in even the most extreme cases; in those, for example, in which the execution of a sentence was stayed until "the prisoner returned to health," i. e., when the person in question had great interest in clinging to his hysterical reactions.

Stier has seen many persons who, when subjected to medical reexamination relative to need for further compensation, again reacted hysterically in the same or almost similar manner as they did at previous examinations. A careful investigation of the interval between medical examinations will reveal that the hysterical reactions were no longer present; that the subjects were able to work and displayed no obvious symptoms.

New conflicts, marital troubles, financial losses or other business cares tend to upset the mental equilibrium once more and usher in hysterical reactions similar to those existing at the time compensation was granted.

Hysterical reactions to accident are almost never seen in persons who are not insured. In persons who are insured one encounters them frequently.

PROF. A. HOCHÉ

Dr. Hoche asks the question, "What evidence exists to support current medical opinion regarding the nature of hysteria?" Previous explanations of hysterical reactions diverge in two directions: (1) analysis of the hysterical personality; (2) analysis of the hysterical symptoms.

Kraepelin's biologic view that hysterical manifestations are primitive defense mechanisms that are set into motion by the instinct of self-preservation and, therefore, observed especially in naive persons, such as children, women and primitive people, has no importance as far as the individual case is concerned despite its scientific interest. Most of the definitions relating to hysteria are of a psychologic character. Möbius considered that hysteria was created by ideas, and later included also that which was produced by affect. Babinski

thought that hysteria was caused by suggestion. Janet's "splitting of consciousness" explained the amnesias, analgesias, etc. The assumption of a psychogenic origin is common to all of these explanations; therefore, for a time, psychogenic was synonymous with hysterical.

A new point of view was ushered in when it was assumed that the motive was important. A moralizing attitude was thus added which today, even more than formerly, stands in the foreground. To this category belongs Jasper's formulations that hysterical persons want to be more than they are and to do more than they are able to accomplish; also Kohnstam's notion of the "inadequate feeling of health," as well as the famous notion regarding the "flight into sickness," which is taken over from the psychoanalysts. These are concepts which, like most attractive formulations, have very little to say from a practical standpoint. The moralizing point of view flourishes especially in the conception of the traumatic neuroses and is observed particularly in the view that considers such psychogenic disorders hysterical, in which an interest or a speculation for producing some external effect in some way operates as a motive, either unconscious or semiconscious in type. It is true that a large number of hysterical manifestations do not appear when there is no one there to witness them; for example, the hysterical attacks. It is not probable that a hermit in the desert or a shipwrecked person on Salas y Gomez would have suffered a hysterical attack, for then perhaps he might have wanted to make an impression on God. Of all the possible views on hysteria that now exist, none is entirely satisfactory. All of them, however, and especially the motive theory, circumvent the decisive point, namely, wherein lies the essential nature of hysteria; what occurs psychologically in hysterical analgesias; in the hysterical paralyses, etc.? For example, if one observes the normal course of events in volitional activities, one sees that the largest part of the path did not appear in consciousness. One is conscious of a definite resolution and a volitional act; then one sees the movement appear at the periphery. About what occurs in the interval one knows nothing, and that is just what one needs most to know. Somewhere on this dark path lies a point where the two series of physical and mental events make contact with each other. Knowledge of the motives behind the symptom does not help. One might ask, wherein lies the difference between a simulated and a hysterical paralysis when the same motive exists, for example, to appear ill. If the will alone can produce such hysterical symptoms it would also be possible to produce the picture of a war tremor voluntarily, and who is able to do that? It is questionable whether the ability to produce hysterical symptoms is a general attribute of the human personality.

It is not even certain whether hysterical manifestations can be set into motion, exclusively, from the mental side. Experience with neuroses following lightning shock and high frequency currents, as well as observations in the war following the effects of shrapnel, situations from which those who were involved awaken with hysterical paralysis without the possibility of having had any opportunity to think or feel about it, might be used in this sense. The dogma concerning the effective influence of a motive of interest in producing neurotic symptoms does not contribute to knowledge of all these difficult questions. Although one might possess the most intimate knowledge of the motives involved, one nevertheless fails to have the slightest understanding of the nature of the process released thereby; and it is a remarkable error when the confirmed champions of this view are of the opinion that they have found the key to the nature of hysteria with the discovery of the motive.

Are there any prospects of ever understanding the true nature of hysteria? These prospects stand or fall with the degree of knowledge concerning the relationship between matter and soul, about which nothing is known. Many theories will come and go, but it is only scientific conceit that will believe in the finality of these episodic points of view. From the practical standpoint, one can, as a rule, recognize cases of hysteria diagnostically with an adequate amount of certainty; but generalizations and conclusions are not permissible which are based

on any of the current conceptions of hysteria. In many and especially the most important points relative to traumatic neuroses, complete unity prevails among medical experts. 1. Everywhere in Germany today, claims are raised and satisfied in cases in which one is convinced that the applicants would be healthy and capable of working if they were not insured. 2. This evil condition is so widespread that urgent relief is necessary. The differences of opinion exist largely as to the manner of bringing about a change in the situation.

Hoche then discusses the psychology of the German Workingmen's Insurance Department; the psychology of the traumatic neurotic patient, and the psychology of the medical expert. Since the onset of its activities, the German Workingmen's Insurance Department has always endeavored to adjust legal and social points of view in an equitable manner. The main emphasis is now placed on the concept of "substantial cause." In the theory of causation, physical, biologic and legal points of view are subject to equal claims, and the physician is not guilty of trespassing beyond his sphere when he takes issue with the legal interpretations of the German Workingmen's Insurance Department. The decisions of this department do not bind the medical expert. In the first place, the decision holds good only for the individual case in which it was rendered.

The medical expert, in sizing up the individual case, is neither protected from nor conscientiously bound by the decisions of the German Workingmen's Insurance Department. As he contributes materially to the theoretical understanding of the traumatic case, he is not only justified but is in duty bound to determine whether the decisions of the German Workingmen's Insurance Department emanate from correct medical opinions.

"The substantial cause" is practically the one point on which the claim for damages is based. The details of the legal theory of causation do not affect the physicians. The physician recognizes in the origin of disease conditions: cause and conditioning factors. Caused by means: "by or through this;" conditioned by means: "not without this." Logically speaking, a causal event is one with which a definite event is necessarily, inseparably, invariably and logically associated. In pathology, the conditions in which these stipulations are fulfilled are in the minority. In general, one has to deal with conditioning factors from whose concurrent or antagonistic forces a biologic cause arises.

In physics, the relationships are simpler. One considers heat as the cause of boiling water; but one also knows that a modifying conditioning factor operates, namely, the barometric pressure, on which depends the height of the boiling point. In the nervous system are found various degrees in the distinctness of the causal relationships. If a radial nerve is severed with a knife and the hand can no longer be raised, then there is a genuine experimental state of affairs which approximates the accurateness of physical causation. Not quite, but almost, as unequivocal is the situation when the pyramidal tract is disturbed by hemorrhage. In both examples the effect always manifests itself in the same way. The demands of theory and experience cover each other. Cause and effect are before one, and there is hardly any influence by conditioning factors. Much more unsurveyable is the causal situation, for example, in dementia paralytica in which progressive mental enfeeblement develops in consequence of the destruction of the cells and fibers of the central nervous system. If one were dealing here purely with cause and effect, the dependence of the symptoms on anatomic changes would be calculable. But it is not known which of the symptoms is referable to actual destruction of the cells, to the effects of poison, to disturbance in circulation, etc. The mutual relationship between cause and conditioning factors appears palpable in toxic disorders. Following an equally prolonged and equally severe poisoning with alcohol, there appear no mental sequelae, delirium tremens, hallucinosis or delusions of infidelity, etc. To be sure, alcohol is necessary for their origin, but it is not an unadulterated cause for that which develops, and is much more a conditioning factor; the other conditioning factors are given in the structure of the personality. Deliria occur also without alcohol.

Conditions become progressively more complicated and unsurveyable as soon as mental factors are added. The accident is never a pure and direct cause for the nervous and mental symptoms of nonorganic type that follow it. The type of reactions of the person involved in an accident is as protean as is normally the varied behavior of the individual person subjected to the blows of fate.

In the traumatic neuroses, the German Workingmen's Insurance Department declines to consider or recognize the accident as a substantial cause—cause not of the illness, but of the incapacity for gainful work. (The Department cleverly avoids the concept of disease here.) One's natural feelings rebel against accepting such a construction, and one cannot help but feel that without the accident the whole mental and legal picture would not have arisen.

Hoche cannot regard the whole theory of causation as held by the German Workingmen's Insurance Department of 1926 in the case of traumatic neuroses as tenable. He tests their premises on an obvious example from organic pathology in the following manner: Today there are strong grounds for assuming that dementia paralytica does not occur without syphilis. This does not mean that dementia paralytica will be a necessary, predestined result of syphilis, because one knows that only from 7 to 10 per cent of all syphilitic patients develop dementia paralytica. In the other 90 or 93 per cent, therefore, a factor *X* exists within the human mechanism which decides whether the spirochetes will affect the brain. This factor *X* is one of the conditioning factors that will determine the number of syphilitic patients who will develop dementia paralytica. The factor *X* alone is incapable by itself of producing dementia paralytica, which, despite all the finesses of the causal theory, requires syphilis as a substantial cause.

If one applies the line of reasoning of the German Workingmen's Insurance Department to this relationship, one would have to say (with slight exaggeration) that syphilis is not a substantial cause of dementia paralytica. One is absolutely right if, speaking purposely in an inexact manner, he says: dementia paralytica is caused by syphilis in the same manner as a neurosis is caused by an accident.

Certainly, the factor *X* decides whether or not nervous manifestations will appear after an accident; but without the accident, the stone would not have begun to roll, and to the impartial person the fact remains: before the accident the individual was a useful citizen, afterward he was not.

Hoche mentions a type of accident case which he calls "nervous." There are numerous disorders which fit neither in the organic nor in the psychogenic (and hysterical) category. These occur in persons, for example, with abnormal sensitivity of the skin to light, insect bites or medicines, or who are abnormally fatigable, dyspeptic or subject to tachycardia, etc. These disorders occur in persons for whose structure Hoche uses the term "inadequacy of tissue vigor." In such personalities primary disease sometimes may appear as reactions to the nonorganic effects of trauma, without wishes and without ideas; they are erroneously classified as psychogenic or hysterical.

In the German Workingmen's Insurance Department of 1926, cases are unjustly excluded in which the patients suffer only from the notion of being ill. This decision unjustly evaluates the effect of the wishes; it underestimates the degree of injury caused by the compensation proceedings.

As far as the psychology of the medical expert is concerned, the reviewer believes that all are inclined to look with displeasure on dealing with the problem of the traumatic neurosis and with the necessity of spending time with neurotic patients. It is with the same feeling of displeasure that section 51 of the criminal law is applied to the group of so-called congenital criminals. As an extreme case exemplifying the mental attitude of some medical experts, mention may be made of the attitude of an insurance physician whom Hoche invited to a hearing while he was chairman of a Compensation Commission. His reply to the invitation to attend was, "That is quite useless, I consider every traumatic neurotic a pig."

Whoever is frank enough to venture an opinion will admit that if, among a number of nervous cases, a damage-suit case is recognized, something emotional at once creeps over him which savors predominantly of an attitude of refusal. This rests in part on the anticipation of a great deal of writing and on the necessity in the expert testimony for constant repetition of a trend of thought that has long been obnoxious; in part, on the anticipation of an unpleasant sensation associated with the task of differentiating simulated from genuine symptoms and having to feel the inner resistance of the object of the examination.

The magnitude of the task of being just at all times will usually be underestimated by those who have slight talent for self-observation. Whoever is accustomed to control his own condition as an examiner or as the chairman of a medical commission is well aware of this. Whoever is honest enough to take stock of himself knows, for example, that the medical expert, according to whether he is called in by one or the other party, feels a semiconscious inclination arising within himself to look on the matter in question in a definite way, an inclination that becomes innocuous at the moment he is conscious of it. As in persons injured, the sensitiveness of the feeling of justice in medical experts is extremely varied. A sensitive feeling of justice will be repelled by judicial decisions which are medically unsatisfactory and will hesitate to confine an opinion to rigid points of view. The more so since theoretical command of the law in no way implies security for the possession of an unclouded feeling of justice.

It is self-evident that there are medical experts who welcome the attitude of the German Workingmen's Insurance Department of 1926 as an agreeable solution of perplexing difficulties. Whoever has learned to consider the mental genesis of convictions has at the outset a suspicious attitude toward every solution that looks too good. Here, too, one will observe that the trend of thought will take the line of least resistance. The maxim holds true in this instance also; namely, whoever generalizes much, errs much.

The danger also exists, and this can be easily shown from the history of medicine, that starting with preconceived notions one is inclined to read into the symptom what he had already theoretically or dogmatically anticipated. The greatest and at the same time the most grotesque example of this process of thinking is given by the psychoanalytic movement, the adherents of which, in large measure, see in the inner life of man whatever is demanded by the dogma of the master, Freud. A particularly good example of the dogmatic bias is Reichardt's opinion that the results of cerebral concussion disappear after such and such length of time, and that all that remains is damage-suit neurosis. A strong dose of belief in one's own infallibility is required to separate every time, with accuracy, neurotic persons from simulators.

Hoche is also of the impression that the official conception of the economic attitude of people in general constructs an ideal type. In the case of a person injured by accident, it all at once becomes a highly objectionable attitude if one begins to think of his own economic advantage. Hoche would like to know what percentage of persons nowadays think of anything else. As medical experts we must not indulge in hypocrisy. We constantly observe that the conscience of most people is subject to wide latitude in regard to money matters when it is not dealing with private individuals but with the State. Of course the few persons who have never given accurate tax declarations or tried to smuggle in cigars over the frontier are of no consequence.

The medical expert must also be cautious about having a punitive attitude toward surly, neurotic patients; in all of us slumbers incurably a bit of the policeman and school-master.

There is no formula for dealing with the complicated problems of the traumatic neurotic patient. Hoche believes that the German Workingmen's Insurance laws are inadequate; that much injustice occurs, and that the belief in justice will suffer as a result.

If the medical expert wishes to be true to his own conscience, his decisions must not lean on the interpretation of a law the inadequacy of which is obvious. The law has created the traumatic neurosis, and the law should remove it.

Hoche offers the suggestion, namely, that those nervous and mental disorders are not eligible for damages which owe their existence not to an accident, as such, but to the fact that the person was insured.

PROF. R. WILMANNS

Westphal and his pupils, especially Oppenheim, pointed out a disease picture that developed immediately after an accident and called it "traumatic neurosis." Oppenheim believed that this neurosis corresponded to insidious organic changes in the central nervous system. Schultze, Strümpell and others disagreed with this view and emphasized the psychogenic origin of the neurotic complaints following an accident.

Charcot looked on the traumatic neuroses as a manifestation of hysteria. Kraepelin called them "fright neuroses" and separated them sharply from hysterical insanity. While neurologists focused their attention on the hysterical paralyses, anesthesia, etc., Kraepelin focused it on the hysterical personality make-up on the basis of which the hysterical symptoms develop. Valuable as Kraepelin's personality studies of hysteria were, there were some important objections to his theory. Experience showed that personalities that corresponded with Kraepelin's hysterical make-up displayed no hysterical states despite the presence of most difficult situations and conflicts, and that hysterical symptoms could develop in persons without the existence of a hysterical personality make-up. In order to save his theory, Kraepelin first assumed that the special hysterical personality need not always be apparent and that a latent hysterical personality could exist; then he separated psychogenic conditions, which arise from definite experiences, fright, trauma, imprisonment, etc., from hysteria. Influenced by these views, Nissl ventured to hope that study of the anatomy of the brain would reveal the cerebral basis for hysterical insanity at some future date. Kraepelin's own pupils objected to these ideas. Even before the World War, the view prevailed, and it is now more or less accepted, that by the old designation, hysteria, one understood those pathologic reactions collectively which developed, on the soil of a so-called hysterical character and the closely related psychopathic constitution, following mental shocks of an objectively trivial nature; but at the same time recognized that the same morbid pictures could arise in other abnormal persons, even in persons who were mentally normal, after mental trauma of particular severity. The experiences of the war gave decisive proof for the correctness of this view.

When Wilmanns visited the Baden military hospitals for the first time during October, 1914, he found about 80 neurotic patients (particularly deaf, aphonic, paralytic, tremulous and stuporous patients) among 40,000 inmates. They had all acquired the war neurosis immediately after fright-producing experiences, such as explosions, burial by débris, etc. Many of them recovered in a short time, but a large number continued unimproved. During the winter of 1914 and 1915, the population in the hospital was increased more and more by these neuroses. The front line medical officers, who at times visited home on furlough, confirmed the prevalence of such fright neuroses in the field hospitals as well, but expressed astonishment over the slight tendency of the patients with fright neuroses to recover near at home in contrast to their rapid course in the field hospitals. Swiss physicians reported that the same condition prevailed in the French hospitals, which at the beginning of 1915 already overflowed with neurotic patients. More striking, too, was the fact that the neuroses were a great rarity in ours as well as the French camps for military prisoners. In the huge camp for military prisoners at Rastatt, an exact investigation revealed the presence of only two or three cases of hysteria. Indeed, among the exchanged military prisoners, who were examined at Constance by Swiss and German physicians, no neuroses were encountered, and one would have to cope with thousands of them if they had been

just as frequent in prison camps as in the military hospitals at home. It was a striking fact, also, that the severely wounded and maimed soldiers did not have neuroses, but, on the contrary, they affected almost exclusively soldiers who were slightly ill, slightly wounded or physically healthy. In addition, the following situation prevailed: In the first few months of the war, one saw almost exclusively acute fright neuroses, "shell shock," as they were called at that time. In the course of time, however, it was observed with increasing frequency that the same symptom pictures developed in soldiers who had hardly become acquainted with the horrors of war; they occurred even in the reserve forces, in companies in which the soldiers were granted furlough, or under the peaceful atmosphere of hospital life in people who had not yet left the vicinity of home. If Karlsruhe was bombed by the enemy, patients with tremors and convulsions appeared, and, peculiarly enough, only among the inmates of hospitals and members of the troops, never among the female nursing personnel and, so far as Wilmanns knows, not among civilians.

All of these facts offer strong support for the views regarding the nature of the traumatic neuroses which began to appear in psychiatry even before the war. If the person who sustained a severe accident was terribly frightened, he occasionally reacted to the traumatic event with an acute fright neurosis, and if this neurosis followed its natural course it would disappear in hours, days or weeks without leaving any residuals. If, however, the natural tendency to recover from the fright neurosis was hindered by the appearance of interests opposing recovery, the neurosis became chronic. Indeed, in numerous cases, one observed that the same disorders could develop insidiously after mild accidents which were in no way associated with severe mental shock. If one transfers these experiences to the war neurosis, obviously, the so-called "shell shock" was the counterpart of the acute fright neurosis; the war neurosis, arising without antecedent, severe, psychic trauma, corresponded to the slowly developing traumatic neurosis. If by degrees one became convinced that the delayed recovery from the acute and insidious development of a chronic traumatic neurosis was to be traced essentially to a wish for damages, which was nourished by compensation laws, then one could interpret the delayed recovery from so-called "shell shock" and the development of similar pictures without antecedent fright-producing war experiences as a neurotic defense reaction against military service.

Although these views may have found wide acceptance in psychiatric circles, they were in no way appreciated by the rank and file of the medical profession. Therefore, one can easily understand why in no other field of military medicine so many medical errors were committed as in the sizing up and treatment of patients with war neuroses. A misconception of these disorders was general. In practically all corps areas, special reading schools were established for the hysterically deaf who, among the ear specialists, were labeled with the term "labyrinth-shock." Hundreds of thousands of patients with psychogenic paralyses were treated with orthopedic apparatus. Hysterical tremors were regarded as a manifestation of a special form of disease of the spinal cord, "insufficiencia vertebrae," and were treated with plaster casts. All therapeutic efforts in cases of hysteria that had been correctly diagnosed were also a failure. A large number of the patients had to be dismissed from military service as completely disabled and were granted high compensation. They comprised over 10 per cent of all persons disabled in the war. Estates were purchased and schools for instruction established to rehabilitate these neurotic soldiers, with the assumption that they were no longer suited for their previous occupation. Attempts to cure neurotic patients in hospitals located in the city by means of friendly encouragement and mild, diversified occupation were practically fruitless. The results became better only when the hospitals were situated in the country and rigid military discipline was instituted.

Only after the use of the faradic current of the older neurologists did at least the immediate therapeutic results become excellent. The results with the faradic current, however, were only transitory, because as soon as the neurotic soldier

was to be pressed into military service again his symptoms reappeared. In most cases, a return to the reserve forces meant a relapse into the old neurotic condition. Investigations conducted in the spring of 1916 showed that of 500 neurotic patients discharged as cured, only 27 ever returned to the front, and of these only 5 were able to engage in full military duty. This result was so discouraging that from then on it was necessary to give up reinstating neurotic soldiers into the army. They were placed in special hospitals in the vicinity of war industrial activities, especially fuse factories, and not discharged from military service. After rehabilitation, hysterical soldiers were immediately placed as full pay workers in the factories. The proportion of neurotic soldiers who were fully recovered was about 97 per cent. Three per cent were discharged with mild neurotic residuals, and about 15 per cent of these were discharged from treatment with partial disability. This favorable result induced the compensation officials to recall all neurotic soldiers who had already been discharged with compensation and subject them to treatment. In consequence of this action, the number of neurotic compensation cases, which in other corps areas amounted to over 10 per cent, fell to about 3.5 per cent in Baden during 1917, when the calling out of troops was in full swing. As the war neurosis was nothing more than the purposeful reaction of a war-weary soldier against military service, one could expect that as soon as the question of such service was no longer present, the neurosis would disappear by virtue of its uselessness. A striking proof for the correctness of this view was given by the inmates of these special hospitals when the revolution broke out. The neurotic inmates, most of whom were admitted from other corps areas, frequently of low morale, many of them frequently punished, recovered over night, revolted and drove away their physicians.

On the basis of his military experience, Wilmanns answers the four questions as follows: (1) No, because other factors are at play. (2) "That neurotic complaints, after a prolonged interval of absence or marked improvement, reappear in the same, similar or quite different manner was often observed. In the early days following the World War, one often observed recovered neurotic patients, who for some reason or other came in conflict with the criminal courts or were detained for criminal investigation or trial, and again displayed attacks of convulsions or tremor. These cases were so numerous that in Baden the Department of Justice requested medical experts to give lectures on the nature of these disorders to the judges. There were other causes, too, especially unemployment, which, in many instances, gave impetus for neurotic persons previously without symptoms to reproduce their former neurotic symptoms and demand compensation. There was no reason, however, to satisfy these demands because the sequelae of war were abolished and other causes had released the disorders." (3) One must take the same stand when nervous manifestations become aggravated after remaining stationary for many years. That the neurosis should become worse for internal reasons over a period of years is excluded after all that has been said about its nature. If aggravation occurs, one can assume with certainty that some unfavorable influence has interfered with the natural tendency of the neurosis to heal, and has given new nourishment to the wish for further compensation. Such unfavorable influences are often due to a social status that is gradually growing worse, to unfavorable medical suggestions, a stirring up of the patient by misguided advisers, etc., all of which incur increased demands for damages. The aggravation of the neurosis after remaining stationary for many years, therefore, does not call for further compensation. (4) This question is the hardest to answer. Experience shows that whenever a person has once received ample compensation he really never loses his complaints again. Even before the war it was recognized that frequent medical examinations were materially to blame for this unfavorable course of the neurosis. The frequent medical examinations repeatedly directed the attention of the patient toward his supposed rights and kept his cupiscent ideas awake. That it was the subsequent examinations that hindered recovery was taught by the vocational bureaus in cases in which the examinations were dispensed with for the sake of economy, and the injured person was assured that he could enjoy

his permanent compensation unmolested. Before the World War, Wilmanns had occasion to examine a number of patients in accident cases who drew compensation over a period of many years without reexamination. They were all healthy and were engaged in gainful occupations. Wilmanns advises the avoidance of reexaminations and suggests that one limit himself to procuring reliable reports concerning the patient's activities. If these show that the injured person is working without complaints, then one is justified in stopping compensation and not before.

Wilmanns states that much as he would like to welcome a definite stand on the part of the law toward the psychogenic results of accident, nevertheless—though not fully sharing the views of Bonhoeffer, Stier and especially Reichardt—he believes that from a practical standpoint the psychogenic results of accident do not render persons eligible for damages. He states this with full realization of doing injustice in exceptional cases, but with the conviction of sacrificing these rare victims in the interests of general public health.

DR. KNOLL

Privy Councillor Dr. Knoll discusses the legal interpretation of the war and traumatic neuroses. By these are understood the mental phenomena following accidents which are not due to simulation, actual organic injury or serious cerebral concussion, but are solely psychogenic reactions to unconscious strivings (wish-tendencies). Knoll discusses the legal attitude toward what constitutes "damage" or injury, disease and disability; also the significance of differences in expert medical opinion and the treatment in chronic traumatic cases.

In chapter 3, Dr. Scholtze discusses the practical evaluation of scientific conclusions regarding the traumatic neuroses.

Chapter 4 gives a general order issued by the German Workingmen's Insurance Department regarding the question of the neuroses.

Chapter 5 discusses the text of pertinent paragraphs from the German Compensation Law and legal decisions relative to traumatic cases.

This book is heartily recommended to physicians engaged in compensation and insurance work; they will find many helpful suggestions. It also deals with matters of interest to the legal profession and public officials who are interested in industrial problems.

ANALYSE DER SUGGESTIVPHÄNOMENE UND THEORIE DER SUGGESTION. By ALEXANDER HERZBERG. Price, 7 marks. Pp. 128. Berlin: S. Karger, 1930.

This monograph begins with a review of different theories of suggestion, which are divided into five groups. Among them, Freud's is mentioned with measured approval. The author next analyzes the process of waking suggestion among a group of normal children who are led to believe by their teacher that they smell a perfume. This, the author argues, is dependent on four groups of factors: the readiness of the disposition to smell; the sensitiveness of the subject to the stimuli of the situation, willingness, habituation and instinctive impulse; the stability of belief produced by the stimulating and inhibiting influence of experience and also instinctive factors, and crowd psychology in itself conditioned by habit and instinctive factors similar to those already mentioned. The author also analyzes an instance of therapeutic suggestion and believes that this is dependent on five factors: the inhibitory effect which the unpleasant sensations of the disease and the treatment have on the voluntary portion of the symptom mechanism; an expectation of cure aroused by a wish for cure and confidence in the physician and treatment; the intensification of the expectation of cure caused by the unpleasantness of the treatment; the belief in the physician's words caused by experience, instinctive factors and wish for cure, and finally the directly inhibitory effect of sympathy and respect on the symptoms, and also the effect of a certain erotic relationship to the physician.

The process of cure by a charlatan by hypnosis and by hypnotic suggestion is analyzed in a similar manner. The author then gives a long list of the numerous factors concerned in suggestion. He divides these into:

- I. Factors arising in the subject.
  - A. Direct factors.
    1. Special or intrinsic factors.
    2. Plastic or transferred factors.
  - B. Indirect factors.
    1. Summation of factors.
    2. Influences of the tendency of dissociation.
- II. Factors arising in the suggestor.
  - A. General suggestiveness.
    1. Skill.
    2. Technical ability.
    3. Profession.
    4. Factors arousing instincts or criticism.
  - B. Special suggestiveness.
- III. Environmental factors.
  1. Effect of expectation.
  2. Dim, colored or confusing illumination.
  3. Presence of a crowd.
  4. Monotonous and injurious sense impressions.
- IV. The content of the foreign suggestion.
- V. The method of the procedure.
  1. Its frequency.
  2. Its capacity to arouse emotion in the subject.
  3. Its probability.
  4. Its emotional tone.
  5. The mediums of expression which arouse appreciative instincts.
  6. Monotony.

The author's theory of suggestion is built on this scheme. The analysis is carried as far as it can be, apparently, on the basis of an atomistic psychology, but the result seems somewhat barren.

CONTRIBUTION À L'ÉTUDE CLINIQUE DE LA STATIQUE ET L'HYPOTONIE MUSCULAIRE. By M. GOPCEVICH; travail du service de M. le Professeur agrégé T. Alajouanine. Price, 40 francs. Pp. 207. Paris: Jouve & Cie, 1930.

This attractive monograph reveals the continuing inspiration of Charles Foix, whose untimely death robbed France of a great clinician. The author carries forward and gives graphic proof of many of the ideas of his master concerning the function of the coordinating centers in the maintenance of equilibrium and concerning the nature of muscular tonus. It is a study in clinical physiology, reenforced by photographs, myograms and foot imprints in normal and pathologic cases. The introduction of new terms and of terms utilized by previous French workers in this field without careful definition of the terms or description of the related phenomena renders the essay somewhat difficult to abstract. Moreover, the complicated nature of the subject and the variations brought about by various combinations of tonic and equilibratory phenomena are apt to be confusing to the beginner.

Essentially, the author indicates tests for muscular hypotonia in various disorders of the nervous system. In the course of his study he was able to distinguish between two fundamental types of muscular activity for the preservation of fixed attitudes, postural tonus and postural reflexes (tonus d'attitude, reflexe

d'attitude). These varied independently in disorders of stability in the upright position due to disease of the cerebrum, cerebellum, spinal cord and peripheral nerves. Hypotonia was markedly affected and not always in predictable fashion by the accompaniment of disequilibrium. The tests utilized were easy to carry out, and usually clear in their indications: palpation of the muscular masses while the subject was standing or kneeling; the posture of the leg and foot when the popliteal space was depressed; the attitude of the body following a push from behind or in front, during squatting, and while bending to the side; the imprint of the foot.

The results from a clinical aspect are of greater value than the attending theoretical discussion, the latter serving to indicate the complex nature of tonus and posture without offering much in the way of clarification. During kneeling, the calf on the hypotonic side is flatter and the hamstring tendons do not stand out in relief. When the popliteal fossa is pressed on, the heel on the hypotonic side remains in contact with the floor. In flexing the trunk laterally, the opposite heel tends to leave the floor. In squatting, the body is bent forward and the heels remain on the floor. The imprint of the foot is broader on the hypotonic side. When pushed forward or back, the patient shifts the foot on the hypotonic side, although if equilibration is affected conditions are reversed.

The author finally distinguishes between three disturbances of posture (*statique*) in the erect station that develop in nervous diseases accompanied by hypotonia, although he admits all degrees of combination: (a) postural hypotonia (*hypotonie d'attitude*), in which the equilibrium may be disturbed by a disorder of the primitive tonus; (b) static disequilibrium (*déséquilibre statique*) due to disturbance of the postural reflexes (*réflexivité d'attitude*), in which hypotonia exaggerates the disequilibrium; (c) ataxic stability (*statique ataxique*) due to simultaneous disturbance of postural tonus and postural reflexes (*tonus d'attitude, réflexe d'attitude*).

READINGS IN PSYCHOLOGY. By RAYMOND HOLDER WHEELER. Price, \$3.75. Pp. 597. New York: Thomas Y. Crowell Company, 1930.

This volume is a collection of papers by various authors, all of which have been published elsewhere. It is presented in book form for the purpose of giving the beginning student in psychology easy access to a selected number of experimental investigations. The following chapter headings indicate the nature of the subjects presented: Group I. Social Behavior: I. The Individual and the Group: An Application of Eight Organismic Laws. II. The Influence of the Group upon Association and Thought. III. Do Groups Think More Efficiently than Individuals? IV. The Nature of Hypnosis: As Indicated by the Presence or Absence of Post-Hypnotic Amnesia and "Rapport."

Group II. Intelligent Behavior: V. Taking the Dogma out of the I.Q. VI. Intelligence as Method of Adaptation. VII. Experimental Studies of Adaptive Behavior in Cats. VIII. The Solving of Problem-Situations by Preschool Children: An Analysis.

Group III. Emotive Behavior: IX. A Case of Dual Personality. X. A Case of "Dementia Praecox": An Illustration of Eight Organismic Laws. XI. A Case of Retarded Development in the Blind. XII. A Study of Fear by Means of the Psychogalvanic Technique. XIII. Animal Behavior and Internal Drives.

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Group VII. The Nervous System: XXVI. Studies of Cerebral Function in Learning VI. The Theory that Synaptic Resistance is Reduced by the Passage of the Nerve Impulse. XXVII. The Early Development of Behavior in "Amblystoma" and in Man. XXVIII. Biological Foundations of Social Integration.

The edition states that the selection of the readings has been determined "first, by what seems to be the dominant interest in psychology at the present time." If this is true, the book fills its purpose excellently, although the reviewer thinks that the title should be "Reading in Behavioristic Psychology," or as the editor calls it, "Organismic Psychology."

For the book itself the reviewer has only praise, but he does think that it is a pity that students who enter the study of psychology because they are interested in why human beings behave as they do should be given as a textbook one that deals as little with the motives and mechanisms which underlie human behavior as this one does. It does not contain any reference to the data compiled by psychoanalysts, and without knowledge of such data no true understanding of human behavior is possible. Surely students in psychology, who at least must be as interested in human behavior as the average person, would benefit greatly from some exposure to the sources from which most knowledge of human behavior has been gained — psychoanalytic researches.

PARALYSE GÉNÉRALE ET MALARIATHERAPIE. By R. LEROY and G. MEDAKOVITCH. With a Preface by Professeur Dr. Wagner-Jauregg. Price, 80 francs. Pp. 480. Paris: Gaston Doin & Cie, 1931.

In this comprehensive monograph the subject of dementia paralytica is taken up from the therapeutic standpoint entirely. While other forms of treatment are considered, stress is laid on the malarial treatment. The book is divided into twenty-six chapters. It takes up the history of the various substances used in the treatment for dementia paralytica, including bacterial products, chemical substances and infectious diseases.

Chapter II gives the frequency, duration and essential characteristics of the spontaneous remissions. Then come chapters on indications and contraindications to malarial therapy, choice of the malarial organism, preservation of the malarial blood, technic, duration of incubation and dosage, and the course of malarial disease. These chapters are extremely comprehensive, and the literature is gone into thoroughly. The results of treatment from practically every country are analyzed. The authors' personal experiences are reported. A special chapter is devoted to the pathology, and the best known articles in the literature are quoted. The authors apparently have done but little work on the pathology themselves, and the literature is quoted without comment. The medicolegal angle is likewise touched on in a special chapter.

While the book adds nothing new, it does provide a collected and comprehensive review of the literature. The bibliography covers more than fifty pages. For this alone the book is worth the price.

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